

A P P L I C A T I O N

for

UNITED STATES LETTERS PATENT

on

1,2-DISUBSTITUTED-6-OXO-3-PHENYL-PIPERIDINE-3-CARBOXAMIDES
AND COMBINATORIAL LIBRARIES THEREOF

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1,2-DISUBSTITUTED-6-OXO-3-PHENYL-PIPERIDINE-3-CARBOXAMIDES.

AND COMBINATORIAL LIBRARIES THEREOF

FIELD OF THE INVENTION

[0001] The present invention relates generally to the synthesis of compounds comprising piperidine-3-carboxamides. In one embodiment, the invention provides novel 1,2-disubstituted-6-oxo-3-phenyl-piperidine-3-carboxamide derivative compounds as well as novel combinatorial libraries comprised of such compounds.

BACKGROUND INFORMATION

[0002] The process of discovering new therapeutically active compounds for a given indication involves the screening of all compounds from available compound collections. From the compounds tested, one or more structures are selected as a promising lead. A large number of related analogs are then synthesized in order to develop a structure-activity relationship and select one or more optimal compounds. With traditional "one-at-a-time" synthesis and biological testing of analogs, this optimization process is long and labor intensive. Adding significant numbers of new structures to the compound collections used in the initial screening step of the discovery and optimization process cannot be accomplished with traditional "one-at-a-time" synthesis methods, except over a time frame of years or even decades. Faster methods are needed that allow for the preparation of up to thousands of related compounds in a matter of days or a few weeks. This need is particularly evident when it comes to synthesizing more complex compounds, such as piperidine-3-carboxamide derivative compounds.

[0003] Combinatorial approaches have been extended to "organic," or non-peptide, libraries. However, the libraries to date contain compounds of limited

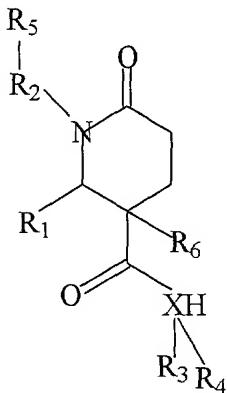
diversity and complexity. A need therefore exists to develop more complex libraries based on medicinal compounds which would need less time and effort in the synthesis and testing required to bring an organic pharmaceutical product to fruition. In short, improved methods for generating therapeutically useful compounds, such as piperidine-3-carboxamide derivatives, are desired.

[0004] Piperidine and carboxamide derivative compounds have been the subject of investigation in a number of different biological areas. For example, piperidine-3-carboxamides have been proposed or used as platelet aggregation inhibitors (Zheng, et al., "Design and synthesis of piperidine-3-carboxamides as human platelet aggregation inhibitor", (1995), Journal of Medicinal Chemistry, vol. 38, No. 1, pp. 180-188) and piperidine derivatives have been proposed as medicaments with rennin inhibiting activity (U.S. Patent No. 6,150,526 issued on November 21, 2000 and U. S. Patent No. 6,051,712 issued on April 18, 2000 both by to Binggeli, et al.)

[0005] This invention satisfies the above discussed need and provides related advantages as well. The present invention overcomes the known limitations to classical serial organic synthesis of piperidine-3-carboxamide derivatives, for example, as well as the shortcomings of combinatorial chemistry related to piperidine-3-carboxamide derivatives. The present invention allows for rapid generation of large diverse libraries of complex piperidine-3-carboxamide derivatives as discrete molecules. The present invention can utilize a readily available pool of building blocks that can be incorporated into the various regions of the molecule. Furthermore, the method of making the present invention allows for the use of building blocks that contain a wide range of diverse functionality. Such building blocks can provide combinatorial libraries that consist of large numbers as well as combinatorial libraries that are extremely diverse with respect to the functionality contained within those libraries. The present invention combines the techniques of solid-phase synthesis of piperidine-3-carboxamide derivatives and the general techniques of synthesis of combinatorial libraries to prepare highly diverse new piperidine-3-carboxamide derivative compounds.

SUMMARY OF THE INVENTION

[0006] The present invention relates to novel piperidine-3-carboxamide derivative compounds of the following formula:



wherein

[0007] X is selected from the group consisting of N and O;

[0008] R₁ is selected from the group consisting of a substituted aromatic heterocyclic ring, C₃-C₁₂ substituted alicycle and substituted phenyl;

[0009] R₂ is selected from the group consisting of H; -OH; C₁ to C₇ alkoxy; C₁ to C₇ substituted alkoxy; C₂-C₇ alkenyl; C₁ to C₇ substituted alkenyl; C₂ to C₇ alkynyl; C₂ to C₇ substituted alkynyl; unsubstituted phenyl; naphthyl; substituted phenoxy; C₂ to C₇ heterocyclic ring; substituted C₂ to C₇ heterocyclic ring; substituted cyclic C₂ to C₇ alkylene; C₁ to C₇ alkyl; C₁ to C₇ substituted alkyl; C₃ to C₇ cycloalkyl; C₃ to C₇ substituted cycloalkyl; C₁ to C₇ alkoxy; halo; C₁ to C₁₀ alkylthio; C₁ to C₁₀ substituted alkylthio; C₁ to C₁₀ alkylnitrile; a C₇ to C₁₈ substituted phenylalkyl; substituted phenyl;

[0010] R₃ and R₄ are independently selected from the group consisting of -OH; H; C₁ to C₆ alkyl; C₁ to C₇ substituted alkyl; C₂ to C₇ alkenyl; C₁ to C₇ alkoxy; C₁ to C₇ substituted alkoxy; C₃ to C₇ cycloalkyl; C₃ to C₇ substituted cycloalkyl; C₁

to C₁₀ alkylthio; C₁ to C₁₀ alkylNitrile; C₁ to C₄ alcohol; substituted phenyl; C₁ to C₆ substituted alkyl; C₁ to C₇ alkoxy; C₃ to C₇ cycloalkyl; and C₃ to C₇ substituted cycloalkyl; C₂ to C₇ heterocyclic ring; C₂ to C₇ substituted heterocyclic ring; phenoxy; and substituted phenoxy,

[0011] R₅ is selected from the group consisting of H and NH₂, and

[0012] R₆ is selected from the group consisting of phenyl, substituted phenyl, C₂ to C₇ heterocyclic ring, and substituted C₂ to C₇ heterocyclic ring.

[0013] The invention further relates to combinatorial libraries containing two or more such compounds, as well as methods of preparing piperidine-3-carboxamide derivative compounds.

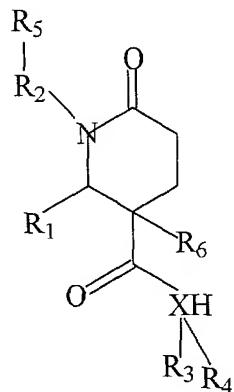
BRIEF DESCRIPTION OF THE DRAWING

[0014] Figures 1 and 2 show two parts of a scheme for the combinatorial synthesis of piperidine-3-carboxamide derivative compounds.

[0015] Figure 3 shows a scheme for the production of (Substituted Phenyl)-glutaric anhydrides.

DETAILED DESCRIPTION OF THE INVENTION

[0016] The present invention provides compounds and combinatorial libraries of compounds of the formula:



wherein:

- [0017] X is selected from the group consisting of N and O;
- [0018] R₁ is selected from the group consisting of a substituted aromatic heterocyclic ring, C₃-C₁₂ substituted alicycle and substituted phenyl;
- [0019] R₂ is selected from the group consisting of H; -OH; C₁ to C₇ alkoxy; C₁ to C₇ substituted alkoxy; C₂-C₇ alkenyl; C₁ to C₇ substituted alkenyl; C₂ to C₇ alkynyl; C₂ to C₇ substituted alkynyl; unsubstituted phenyl; naphthyl; substituted phenoxy; C₂ to C₇ heterocyclic ring; substituted C₂ to C₇ heterocyclic ring; substituted cyclic C₂ to C₇ alkylene; C₁ to C₇ alkyl; C₁ to C₇ substituted alkyl; C₃ to C₇ cycloalkyl; C₃ to C₇ substituted cycloalkyl; C₁ to C₇ alkoxy; halo; C₁ to C₁₀ alkylthio; C₁ to C₁₀ substituted alkylthio; C₁ to C₁₀ alkylitrile; a C₇ to C₁₈ substituted phenylalkyl; substituted phenyl;
- [0020] R₃ and R₄ are independently selected from the group consisting of -OH; H; C₁ to C₆ alkyl; C₁ to C₇ substituted alkyl; C₂ to C₇ alkenyl; C₁ to C₇ alkoxy; C₁ to C₇ substituted alkoxy; C₃ to C₇ cycloalkyl; C₃ to C₇ substituted cycloalkyl; C₁ to C₁₀ alkylthio; C₁ to C₁₀ alkylitrile; C₁ to C₄ alcohol; substituted phenyl; C₁ to C₆ substituted alkyl; C₁ to C₇ alkoxy; C₃ to C₇ cycloalkyl; and C₃ to C₇ substituted cycloalkyl; C₂ to C₇ heterocyclic ring; C₂ to C₇ substituted heterocyclic ring; phenoxy; and substituted phenoxy,
- [0021] R₅ is selected from the group consisting of H and NH₂, and
- [0022] R₆ is selected from the group consisting of phenyl, substituted phenyl, C₂ to C₇ heterocyclic ring, and substituted C₂ to C₇ heterocyclic ring.
- [0023] The invention also provides methods of preparing piperidine-3-carboxamide derivative compounds and combinatorial libraries. In one method, as shown in Figures 1 and 2, such compounds can be prepared by a process comprising:
- [0024] preparing a resin bound aldehyde or diamine,
- [0025] reacting said resin bound aldehyde with an amine, or said resin bound diamine with an aldehyde, to form a resin bound imine,
- [0026] cyclizing said resin bound imine to produce a resin bound carboxylic acid,

[0027] acylating said resin bound carboxylic acid, and

[0028] cleaving and extracting said piperidine-3-carboxamide derivative compound from said resin.

[0029] Examples of aldehydes which are useful in the above reaction include but are not limited to 4-hydroxybenzaldehyde, 3-hydroxybenzaldehyde, 2-hydroxy-5-methylbenzaldehyde, 3,5-dimethyl-4-hydroxybenzaldehyde, 2-hydroxy-4-methoxybenzaldehyde, 3-ethoxysalicylaldehyde, 2-hydroxy-1-naphthaldehyde, 5-bromosalicylaldehyde, cyclopropanecarboxaldehyde, 3-furaldehyde, benzaldehyde, 2-thiophenecarboxaldehyde, 3-thiophenecarboxaldehyde, P-tolualdehyde, 4,5-dimethyl-2-furancarboxaldehyde, P-anisaldehyde, 5-methylfurfural, O-tolualdehyde, 2,4,5-trimethylbenzaldehyde, piperonal, 5-methyl-2-thiophenecarboxaldehyde, 4-(difluoromethoxy)benzaldehyde, 5-bromo-2-furaldehyde, 4-biphenylcarboxaldehyde and 5-bromo-2-thiophenecarboxaldehyde.

[0030] Examples of diamines and amines useful in the above reaction when producing a resin bound diamine or reaction an aldehyde with an amine, include but are not limited to methylamine, ethylamine, propargylamine, cyclopropylamine, allylamine, propylamine, 3-aminopropionitrile, isobutylamine, cyclopentylamine, cyclohexylamine, hexylamine, N-acetylenediamine, 3-ethoxypropylamine, 4-chlorobenzylamine, 1-(3-aminopropyl)-2-pyrrolidinone, tryptamine, 3-(trifluoromethyl)benzylamine, 2,4-diclorophenethylamine, 4-amino-1-benzylpiperidine, benzylamine, ethylenediamine, 1,3-diaminopropane, 1,4-diaminobutane, trans-1,2-cyclohexanediamine, trans-1,4-diaminocyclohexane, 2,2-thiobis(ethylamine), and N,N-Bis(3-aminopropyl)methylamine.

[0031] Examples of amines useful in the above reaction when acylating the resin bound carboxylic acid include but are not limited to nipecotamide, 1-(2-aminoethyl)pyrrolidine, pyrrolidine, histamine, cyclopentylamine, allylamine, 2-methoxyethylamine, cyclohexylamine, 1-methylpiperazine, tetrahydrofurfurylamine, 4-methylbenzylamine, 3-fluorobenzylamine, 4-fluorobenzylamine, 1-(3-aminopropyl)imidazole, cyclopropylamine, propylamine, ethanolamine, 2-thiophenemethylamine, n,n-dimethyl-1,3-propanediamine, 1-(2-

aminoethyl)piperidine, isoamylamine, 3-ethoxypropylamine, (r)-(-)-1-cyclohexylethylamine, neopentylamine, 3-(methylthio)propylamine, isobutylamine, 3-amino-1-propanol, 2-ethoxyethylamine, 2,6-dimethylpiperazine, propargylamine, thiophene-2-ethylamine, butylamine, 2-amino-1-methoxypropane, 3-aminopropionitrile, 3-methylpiperidine, P-anisidine, 1,2,3,6-tetrahydropyridine, 2,6-dimethylmorpholine, methoxyamine hydrochloride, n-ethylpiperazine, water, and hydroxylamine.

[0032] When the above-described compounds include one or more chiral centers, the stereochemistry of such chiral centers can independently be in the R or S configuration, or a mixture of the two. The chiral centers can be further designated as R or S or R,S or d,D, I,L or d,I, D,L.

[0033] In the above formula , the term "C₁ to C₇ alkyl" denotes such radicals as methyl, ethyl, n-propyl, isopropyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, amyl, tert-amyl, hexyl and the like. The preferred "C₁ to C₇ alkyl" groups are methyl, iso-butyl, sec-butyl and iso-propyl.

[0034] The term "C₁ to C₇ substituted alkyl," denotes that the above C₁ to C₇ alkyl groups are substituted by one or more, and preferably one or two, halogen, hydroxy, protected hydroxy, oxo, protected oxo, C₃ to C₇ cycloalkyl, naphthyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, guanidino, protected guanidino, heterocyclic ring, substituted heterocyclic ring, imidazolyl, indolyl, pyrrolidinyl, C₁ to C₇ alkoxy, C₁ to C₇ acyl, C₁ to C₇ acyloxy, nitro, carboxy, protected carboxy, carbamoyl, carboxamide, protected carboxamide, N-(C₁ to C₆ alkyl)carboxamide, protected N-(C₁ to C₆ alkyl)carboxamide, N,N-di(C₁ to C₆ alkyl)carboxamide, cyano, methylsulfonylamino, thiol, C₁ to C₄ alkylthio or C₁ to C₄ alkylsulfonyl groups. The substituted alkyl groups may be substituted once or more, and preferably once or twice, with the same or with different substituents.

[0035] Examples of the above substituted alkyl groups include the 2-oxo-prop-1-yl, 3-oxo-but-1-yl, cyanomethyl, nitromethyl, chloromethyl, hydroxymethyl, tetrahydropyranoxymethyl, trityloxymethyl, propionyloxymethyl, amino, methylamino, aminomethyl, dimethylamino, carboxymethyl,

allyloxycarbonylmethyl, allyloxycarbonylaminomethyl, methoxymethyl, ethoxymethyl, t-butoxymethyl, acetoxymethyl, chloromethyl, bromomethyl, iodomethyl, trifluoromethyl, 6-hydroxyhexyl, 2,4-dichloro(n-butyl), 2-aminopropyl, 1-chloroethyl, 2-chloroethyl, 1- bromoethyl, 2-chloroethyl, 1-fluoroethyl, 2-fluoroethyl, 1- iodoethyl, 2-iodoethyl, 1-chloropropyl, 2-chloropropyl, 3-chloropropyl, 1-bromopropyl, 2-bromopropyl, 3-bromopropyl, 1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, 1- iodopropyl, 2-iodopropyl, 3-iodopropyl, 2-aminoethyl, 1- aminoethyl, N-benzoyl-2-aminoethyl, N-acetyl-2-aminoethyl, N-benzoyl-1-aminoethyl, N-acetyl-1-aminoethyl and the like.

[0036] The term "C₁ to C₇ alkoxy" as used herein denotes groups such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, t-butoxy and like groups. A preferred alkoxy is methoxy. The term "C₁ to C₇ substituted alkoxy" means the alkyl portion of the alkoxy can be substituted in the same manner as in relation to C₁ to C₇ substituted alkyl. Similarly, the term "C₁ to C₇ phenylalkoxy" as used herein means "C₁ to C₇ alkoxy" bonded to a phenyl radical.

[0037] The substituent term "C₃ to C₇ cycloalkyl" includes the cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl rings. The substituent term "C₃ to C₇ substituted cycloalkyl" indicates the above cycloalkyl rings substituted by one or two halogen, hydroxy, protected hydroxy, C₁ to C₄ alkylthio, C₁ to C₄ alkylsulfoxide, C₁ to C₄ alkylsulfonyl, C₁ to C₄ substituted alkylthio, C₁ to C₄ substituted alkylsulfoxide, C₁ to C₄ substituted alkylsulfonyl, C₁ to C₆ alkyl, C₁ to C₇ alkoxy, C₁ to C₆ substituted alkyl, C₁ to C₇ alkoxy, oxo, protected oxo, (monosubstituted)amino, (disubstituted)amino, trifluoromethyl, carboxy, protected carboxy, phenyl, substituted phenyl, phenylthio, phenylsulfoxide, phenylsulfonyl, amino, or protected amino groups.

[0038] The term "substituted phenyl" specifies a phenyl group substituted with one or more, and preferably one or two, moieties chosen from the groups consisting of halogen, hydroxy, protected hydroxy, cyano, nitro, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₁ to C₇ alkoxy, C₁ to C₇ substituted alkoxy, C₁ to C₇ acyl, C₁ to C₇ substituted acyl, C₁ to C₇ alkylthio, C₁ to C₇ acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected

hydroxymethyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, carboxamide, protected carboxamide, N-(C₁ to C₆ alkyl)carboxamide, protected N-(C₁ to C₆ alkyl)carboxamide, N, N-di(C₁ to C₆ alkyl)carboxamide, trifluoromethyl, N-(C₁ to C₆ alkyl)sulfonyl)amino, -(phenylsulfonyl)amino or phenyl, wherein the phenyl is substituted or unsubstituted, such that, for example, a biphenyl results.

[0039] Examples of the term "substituted phenyl" includes a mono- or di(halo)phenyl group such as 2, 3 or 4-chlorophenyl, 2,6-dichlorophenyl, 2,5-dichlorophenyl, 3,4-dichlorophenyl, 2, 3 or 4-bromophenyl, 3,4-dibromophenyl, 3-chloro-4-fluorophenyl, 2, 3 or 4-fluorophenyl and the like; a mono or di(hydroxy)phenyl group such as 2, 3 or 4-hydroxyphenyl, 2,4-dihydroxyphenyl, the protected-hydroxy derivatives thereof and the like; a nitrophenyl group such as 2, 3 or 4-nitrophenyl; a cyanophenyl group, for example, 2, 3 or 4-cyanophenyl; a mono- or di(alkyl)phenyl group such as 2, 3 or 4-methylphenyl, 2,4-dimethylphenyl, 2, 3 or 4-(iso-propyl)phenyl, 2, 3 or 4-ethylphenyl, 2, 3 or 4-(n-propyl)phenyl and the like; a mono or di(alkoxyl)phenyl group, for example, 2,6-dimethoxyphenyl, 2, 3 or 4-methoxyphenyl, 2, 3 or 4-ethoxyphenyl, 2, 3 or 4-(isopropoxy)phenyl, 2, 3 or 4-(t-butoxy)phenyl, 3-ethoxy-4-methoxyphenyl and the like; 2, 3 or 4-trifluoromethylphenyl; a mono- or dicarboxyphenyl or (protected carboxy)phenyl group such as 2, 3 or 4-carboxyphenyl or 2,4-di(protected carboxy)phenyl; a mono- or di(hydroxymethyl)phenyl or (protected hydroxymethyl)phenyl such as 2, 3, or 4-(protected hydroxymethyl)phenyl or 3,4-di(hydroxymethyl)phenyl; a mono- or di(aminomethyl)phenyl or (protected aminomethyl)phenyl such as 2, 3 or 4-(aminomethyl)phenyl or 2,4-(protected aminomethyl)phenyl; or a mono- or di(N-(methylsulfonylamino))phenyl such as 2, 3 or 4-(N-(methylsulfonylamino))phenyl. Also, the term "substituted phenyl" represents disubstituted phenyl groups wherein the substituents are different, for example, 3-methyl-4-hydroxyphenyl, 3-chloro-4-hydroxyphenyl, 2-methoxy-4-bromophenyl, 4-ethyl-2-hydroxyphenyl, 3-hydroxy-4-nitrophenyl, 2-hydroxy-4-chlorophenyl and the like.

[0040] The terms "halo" and "halogen" refer to the fluoro, chloro, bromo or

iodo atoms. There can be one or more halogen, which are the same or different. Preferred halogens are chloro and fluoro.

[0041] The term "substituted amino" refers to an amino group with one substituent chosen from the group consisting of phenyl, substituted phenyl, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₁ to C₇ acyl, C₁ to C₇ substituted acyl, C₂ to C₇ alkenyl, C₂ to C₇ substituted alkenyl, C₂ to C₇ alkynyl, C₂ to C₇ substituted alkynyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ substituted phenylalkyl and heterocyclic ring. The substituted amino can additionally have an amino-protecting group as encompassed by the term "protected substituted amino."

[0042] The term "(disubstituted)amino" refers to an amino group with two substituents chosen from the group consisting of phenyl, substituted phenyl, C₁ to C₆ alkyl, C₁ to C₆ substituted alkyl, C₁ to C₇ acyl, C₂ to C₇ alkenyl, C₂ to C₇ alkynyl, C₇ to C₁₂ phenylalkyl, and C₇ to C₁₂ substituted phenylalkyl. The two substituents can be the same or different.

[0043] The term "C₁ to C₄ alkylthio" refers to sulfide groups such as methylthio, ethylthio, n-propylthio, isopropylthio, n-butylthio, t-butylthio and like groups.

[0044] The term "C₁ to C₄ substituted alkylthio," denotes that the C₁ to C₄ alkyl portion of this group may be substituted as described above in relation to "substituted alkyl."

[0045] The term "phenoxy" denotes a phenyl bonded to an oxygen atom, wherein the binding to the rest of the molecule is through the oxygen atom. The term "substituted phenoxy" specifies a phenoxy group substituted with one or more, and preferably one or two, moieties chosen from the groups consisting of halogen, hydroxy, protected hydroxy, cyano, nitro, C₁ to C₁₂ alkyl, C₁ to C₁₂ alkoxy, C₁ to C₁₂ substituted alkoxy, C₁ to C₁₂ acyl, C₁ to C₁₂ acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, carboxamide, protected carboxamide, N-(C₁ to C₁₂ alkyl)carboxamide, protected N-(C₁ to C₁₂ alkyl)carboxamide, N, N-di(C₁ to C₁₂ alkyl)carboxamide, trifluoromethyl, N-((C₁ to

C_{12} alkyl)sulfonyl)amino and N-(phenylsulfonyl)amino.

[0046] The terms "C₇ to C₁₈ substituted phenylalkyl" and "C₁ to C₁₂ substituted heterocycloalkyl" denote a C₇ to C₁₈ phenylalkyl group or C₁ to C₁₂ heterocycloalkyl substituted (on the alkyl or, where applicable, phenyl or heterocyclic portion) with one or more, and preferably one or two, groups chosen from halogen, hydroxy, protected hydroxy, oxo, protected oxo, amino, protected amino, substituted amino, protected substituted amino, (disubstituted)amino, guanidino, protected guanidino, heterocyclic ring, substituted heterocyclic ring, C₁ to C₁₂ alkyl, C₁ to C₁₂ substituted alkyl, C₁ to C₁₂ alkoxy, C₁ to C₁₂ substituted alkoxy, C₁ to C₁₂ acyl, C₁ to C₁₂ substituted acyl, C₁ to C₁₂ acyloxy, nitro, carboxy, protected carboxy, carbamoyl, carboxamide, protected carboxamide, N-(C₁ to C₁₂ alkyl)carboxamide, protected N-(C₁ to C₁₂ alkyl)carboxamide, N, N-(C₁ to C₁₂ dialkyl)carboxamide, cyano, N-(C₁ to C₁₂ alkylsulfonyl)amino, thiol, C₁ to C₁₀ alkylthio, C₁ to C₁₀ alkylsulfonyl groups; and/or the phenyl group may be substituted with one or more, and preferably one or two, substituents chosen from halogen, hydroxy, protected hydroxy, cyano, nitro, C₁ to C₁₂ alkyl, C₁ to C₁₂ substituted alkyl, C₁ to C₁₂ alkoxy, C₁ to C₁₂ substituted alkoxy, C₁ to C₁₂ acyl, C₁ to C₁₂ substituted acyl, C₁ to C₁₂ acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, carboxamide, protected carboxamide, N-(C₁ to C₁₂ alkyl)carboxamide, protected N-(C₁ to C₁₂ alkyl)carboxamide, N, N-di(C₁ to C₁₂ alkyl)carboxamide, trifluoromethyl, N-((C₁ to C₁₂ alkyl)sulfonyl)amino, N-(phenylsulfonyl)amino, cyclic C₂ to C₁₂ alkylene or a phenyl group, substituted or unsubstituted, for a resulting biphenyl group. The substituted alkyl, phenyl or heterocyclic groups may be substituted with one or more, and preferably one or two, substituents which can be the same or different.

[0047] Examples of the term "C₇ to C₁₈ substituted phenylalkyl" include groups such as 2-phenyl-1-chloroethyl, 2-(4-methoxyphenyl)ethyl, 4-(2,6-dihydroxy phenyl)n-hexyl, 2-(5-cyano-3-methoxyphenyl)n-pentyl, 3-(2,6-dimethylphenyl)n-propyl, 4-chloro-3-aminobenzyl, 6-(4-methoxyphenyl)-3-carboxy(n-hexyl), 5-(4-

aminomethylphenyl)- 3-(aminomethyl)n-pentyl, 5-phenyl-3-oxo-n-pent-1-yl and the like.

[0048] The term "C₇ to C₁₈ phenylalkylene" specifies a C₇ to C₁₈ phenylalkyl, as defined above, where the phenylalkyl radical is bonded at two different positions connecting together two separate additional groups. The definition includes groups of the formula: -phenyl-alkyl-, -alkyl-phenyl- and -alkyl-phenyl-alkyl-. Substitutions on the phenyl ring can be 1,2, 1,3 or 1,4.

[0049] C₇ to C₁₈ phenylalkylenes include, for example, 1,4-tolylene and 1,3-xylylene.

[0050] The terms "cyclic C₂ to C₇ alkylene," "substituted cyclic C₂ to C₇ alkylene," "cyclic C₂ to C₇ heteroalkylene," and "substituted cyclic C₂ to C₇ heteroalkylene," defines such a cyclic group bonded ("fused") to the phenyl radical resulting in a bicyclic ring system. The cyclic group may be saturated or contain one or two double bonds. Furthermore, the cyclic group may have one or two methylene or methine groups replaced by one or two oxygen, nitrogen or sulfur atoms which are the cyclic C₂ to C₇ heteroalkylene.

[0051] The cyclic alkylene or heteroalkylene group may be substituted once or twice by the same or different substituents which, if appropriate, can be connected to another part of the compound (e.g., alkylene) selected from the group consisting of the following moieties: hydroxy, protected hydroxy, carboxy, protected carboxy, oxo, protected oxo, C₁ to C₄ acyloxy, formyl, C₁ to C₁₂ acyl, C₁ to C₁₂ alkyl, C₁ to C₇ alkoxy, C₁ to C₁₀ alkylthio, C₁ to C₁₀ alkylsulfoxide, C₁ to C₁₀ alkylsulfonyl, halo, amino, protected amino, substituted amino, protected substituted amino, (disubstituted)amino, hydroxymethyl or a protected hydroxymethyl.

[0052] The cyclic alkylene or heteroalkylene group fused onto the benzene radical can contain two to ten ring members, but it preferably contains three to six members. Examples of such saturated cyclic groups are when the resultant bicyclic ring system is 2,3-dihydro-indanyl and a tetralin ring. When the cyclic groups are unsaturated, examples occur when the resultant bicyclic ring system is a naphthyl ring or indolyl. Examples of fused cyclic groups which each contain

one nitrogen atom and one or more double bond, preferably one or two double bonds, are when the benzene radical is fused to a pyridino, pyrano, pyrrolo, pyridinyl, dihydropyrrolo, or dihydropyridinyl ring. Examples of fused cyclic groups which each contain one oxygen atom and one or two double bonds are when the benzene radical ring is fused to a furo, pyrano, dihydrofuran, or dihydropyrano ring. Examples of fused cyclic groups which each have one sulfur atom and contain one or two double bonds are when the benzene radical is fused to a thieno, thiopyrano, dihydrothieno or dihydrothiopyrano ring. Examples of cyclic groups which contain two heteroatoms selected from sulfur and nitrogen and one or two double bonds are when the benzene radical ring is fused to a thiazolo, isothiazolo, dihydrothiazolo or dihydroisothiazolo ring. Examples of cyclic groups which contain two heteroatoms selected from oxygen and nitrogen and one or two double bonds are when the benzene ring is fused to an oxazolo, isoxazolo, dihydrooxazolo or dihydroisoxazolo ring. Examples of cyclic groups which contain two nitrogen heteroatoms and one or two double bonds occur when the benzene ring is fused to a pyrazolo, imidazolo, dihydropyrazolo or dihydroimidazolo ring or pyrazinyl.

[0053] The term "heterocycle" or "heterocyclic ring" denotes optionally substituted five-membered to eight-membered rings that have 1 to 4 heteroatoms, such as oxygen, sulfur and/or nitrogen, in particular nitrogen, either alone or in conjunction with sulfur or oxygen ring atoms. These five-membered to eight-membered rings may be saturated, fully unsaturated or partially unsaturated, with fully saturated rings being preferred. Preferred heterocyclic rings include morpholino, piperidinyl, piperazinyl, 2-amino-imidazoyl, tetrahydrofuran, pyrrolo, tetrahydrothiophen-yl, hexylmethylenimino and heptylmethylenimino.

[0054] The term "substituted heterocycle" or "substituted heterocyclic ring" means the above-described heterocyclic ring is substituted with, for example, one or more, and preferably one or two, substituents which are the same or different which substituents can be halogen, hydroxy, protected hydroxy, cyano, nitro, C₁ to C₁₂ alkyl, C₁ to C₁₂ alkoxy, C₁ to C₁₂ substituted alkoxy, C₁ to C₁₂ acyl,

C₁ to C₁₂ acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, substituted amino, protected substituted amino, (disubstituted)amino carboxamide, protected carboxamide, N-(C₁ to C₁₂ alkyl)carboxamide, protected N-(C₁ to C₁₂ alkyl)carboxamide, N, N-di(C₁ to C₁₂ alkyl)carboxamide, trifluoromethyl, N-((C₁ to C₁₂ alkyl)sulfonyl)amino, N-(phenylsulfonyl)amino, heterocycle or substituted heterocycle groups.

[0055] One or more of the compounds of the invention, even within a given library, may be present as a salt. The term "salt" encompasses those salts that form with the carboxylate anions and amine nitrogens and include salts formed with the organic and inorganic anions and cations discussed below. Furthermore, the term includes salts that form by standard acid-base reactions with basic groups (such as amino groups) and organic or inorganic acids. Such acids include hydrochloric, sulfuric, phosphoric, acetic, succinic, citric, lactic, maleic, fumaric, palmitic, cholic, pamoic, mucic, D-glutamic, D-camphoric, glutaric, phthalic, tartaric, lauric, stearic, salicyclic, methanesulfonic, benzenesulfonic, sorbic, picric, benzoic, cinnamic, and like acids.

[0056] The term "organic or inorganic cation" refers to counter-ions for the carboxylate anion of a carboxylate salt. The counter-ions are chosen from the alkali and alkaline earth metals, (such as lithium, sodium, potassium, barium, aluminum and calcium); ammonium and mono-, di- and tri-alkyl amines such as trimethylamine, cyclohexylamine; and the organic cations, such as dibenzylammonium, benzylammonium, 2-hydroxyethylammonium, bis(2-hydroxyethyl)ammonium, phenylethylbenzylammonium, dibenzylethylenediammonium, and like cations. See, for example, "Pharmaceutical Salts," Berge et al., J. Pharm. Sci., 66:1-19 (1977). Other cations encompassed by the above term include the protonated form of procaine, quinine and N-methylglucosamine, and the protonated forms of basic amino acids such as glycine, ornithine, histidine, phenylglycine, lysine and arginine. Furthermore, any zwitterionic form of the instant compounds formed by a carboxylic acid and an amino group is referred to by this term. For example, a

cation for a carboxylate anion will exist when R₂ or R₃ is substituted with a (quaternary ammonium)methyl group. A preferred cation for the carboxylate anion is the sodium cation.

[0057] The compounds of the invention can also exist as solvates and hydrates. Thus, these compounds may crystallize with, for example, waters of hydration, or one, a number of, or any fraction thereof of molecules of the mother liquor solvent. The solvates and hydrates of such compounds are included within the scope of this invention.

[0058] One or more compounds of the invention, even when in a library, can be in the biologically active ester form, such as the non-toxic, metabolically-labile ester-form. Such ester forms induce increased blood levels and prolong the efficacy of the corresponding non-esterified forms of the compounds. Ester groups which can be used include the lower alkoxyethyl groups, for example, methoxymethyl, ethoxymethyl, isopropoxymethyl and the like; the -(C₁ to C₇) alkoxyethyl groups, for example methoxyethyl, ethoxyethyl, propoxyethyl, isopropoxyethyl and the like; the 2-oxo-1,3-dioxolen-4-ylmethyl groups, such as 5-methyl-2-oxo-1,3-dioxolen-4-ylmethyl, 5-phenyl-2-oxo-1,3-dioxolen-4-ylmethyl and the like; the C₁ to C₄ alkylthiomethyl groups, for example methylthiomethyl, ethylthiomethyl, iso-propylthiomethyl and the like; the acyloxymethyl groups, for example pivaloyloxymethyl, pivaloyloxyethyl, -acetoxyethyl and the like; the ethoxycarbonyl-1-methyl group; the -acetoxyethyl; the 1-(C₁ to C₇) alkyloxycarbonyloxyethyl groups such as the 1-(ethoxycarbonyloxy)ethyl group; and the 1-(C₁ to C₇) alkylaminocarbonyloxyethyl groups such as the 1-(methylaminocarbonyloxy)ethyl group.

[0059] The term "amino acid" includes any one of the twenty naturally-occurring amino acids or the D-form of any one of the naturally-occurring amino acids. In addition, the term "amino acid" also includes other non-naturally occurring amino acids besides the D-amino acids, which are functional equivalents of the naturally-occurring amino acids. Such non-naturally-occurring amino acids include, for example, norleucine ("Nle"), norvaline ("Nva"), L- or D-naphthalanine, ornithine ("Orn"), homoarginine (homoArg) and others well known

in the peptide art, such as those described in M. Bodanzsky, "Principles of Peptide Synthesis," 1st and 2nd revised ed., Springer-Verlag, New York, NY, 1984 and 1993, and Stewart and Young, "Solid Phase Peptide Synthesis," 2nd ed., Pierce Chemical Co., Rockford, IL, 1984. Amino acids and amino acid analogs can be purchased commercially (Sigma Chemical Co.; Advanced Chemtech) or synthesized using methods known in the art.

[0060] The term "functionalized resin" means any resin, crosslinked or otherwise, where functional groups have been introduced into the resin, as is common in the art. Such resins include, for example, those functionalized with amino, alkylhalo, formyl or hydroxy groups. Such resins which can serve as solid supports are well known in the art and include, for example, 4-methylbenzhydrylamine-copoly(styrene-1% divinylbenzene) (MBHA), 4-hydroxymethylphenoxyethyl-copoly(styrene-1% divinylbenzene), 4-oxymethyl-phenyl-acetamido-copoly(styrene-1% divinylbenzene)(Wang), 4-(oxymethyl)-phenylacetamido methyl (Pam), and TentagelTM, from Rapp Polymere GmbH, trialkoxy-diphenyl-methyl ester- copoly(styrene-1% divinylbenzene)(RINK) all of which are commercially available. Other functionalized resins are known in the art and can be used without departure from the scope of the current invention. Such resins may include those described in Jung, G., Combinatorial Peptide and Nonpeptide Libraries, A Handbook (VCH Verlag, 1996) or Bunin, B. A., The Combinatorial Index (Academic Press, 1998).

[0061] As used herein, a "combinatorial library" is an intentionally created collection of differing molecules which can be prepared by the means provided below or otherwise and screened for biological activity in a variety of formats (e.g., libraries of soluble molecules, libraries of compounds attached to resin beads, silica chips or other solid supports). A "combinatorial library," as defined above, involves successive rounds of chemical syntheses based on a common starting structure. The combinatorial libraries can be screened in any variety of assays, such as those detailed below as well as others useful for assessing their biological activity. The combinatorial libraries will generally have at least one active compound and are generally prepared such that the compounds are in

equimolar quantities.

[0062] A combinatorial library of the invention can contain one or more of the above-described compounds. The invention further provides a combinatorial library containing five or more of the above-described compounds. In another embodiment of the invention, a combinatorial library can contain ten or more of the above-described compounds. In yet another embodiment of the invention, a combinatorial library can contain fifty or more of the above-described compounds. If desired, a combinatorial library of the invention can contain 100,000 or more, or even 1,000,000 or more, of the above-described compounds.

[0063] By way of example, the preparation of the combinatorial libraries can use the "split resin approach." The split resin approach is described by, for example, U.S. Patent 5,010,175 to Rutter, WO PCT 91/19735 to Simon, and Gallop et al., *J. Med. Chem.*, 37:1233-1251 (1994).

[0064] For preparing pharmaceutical compositions containing compounds of the invention, inert, pharmaceutically acceptable carriers are used. The pharmaceutical carrier can be either solid or liquid. Solid form preparations include, for example, powders, tablets, dispersible granules, capsules, cachets, and suppositories.

[0065] A solid carrier can be one or more substances which can also act as diluents, flavoring agents, solubilizers, lubricants, suspending agents, binders, or tablet disintegrating agents; it can also be an encapsulating material.

[0066] In powders, the carrier is generally a finely divided solid which is in a mixture with the finely divided active component. In tablets, the active compound is mixed with the carrier having the necessary binding properties in suitable proportions and compacted in the shape and size desired.

[0067] For preparing pharmaceutical composition in the form of suppositories, a low-melting wax such as a mixture of fatty acid glycerides and cocoa butter is first melted and the active ingredient is dispersed therein by, for example, stirring. The molten homogeneous mixture is then poured into convenient-sized molds and allowed to cool and solidify.

[0068] Powders and tablets preferably contain between about 5% to about 70% by weight of the active ingredient. Suitable carriers include, for example, magnesium carbonate, magnesium stearate, talc, lactose, sugar, pectin, dextrin, starch, tragacanth, methyl cellulose, sodium carboxymethyl cellulose, a low-melting wax, cocoa butter and the like.

[0069] The pharmaceutical compositions can include the formulation of the active compound with encapsulating material as a carrier providing a capsule in which the active component (with or without other carriers) is surrounded by a carrier, which is thus in association with it. In a similar manner, cachets are also included. Tablets, powders, cachets, and capsules can be used as solid dosage forms suitable for oral administration.

[0070] Liquid pharmaceutical compositions include, for example, solutions suitable for oral or parenteral administration, or suspensions, and emulsions suitable for oral administration. Sterile water solutions of the active component or sterile solutions of the active component in solvents comprising water, ethanol, or propylene glycol are examples of liquid compositions suitable for parenteral administration.

[0071] Sterile solutions can be prepared by dissolving the active component in the desired solvent system, and then passing the resulting solution through a membrane filter to sterilize it or, alternatively, by dissolving the sterile compound in a previously sterilized solvent under sterile conditions.

[0072] Aqueous solutions for oral administration can be prepared by dissolving the active compound in water and adding suitable flavorants, coloring agents, stabilizers, and thickening agents as desired. Aqueous suspensions for oral use can be made by dispersing the finely divided active component in water together with a viscous material such as natural or synthetic gums, resins, methyl cellulose, sodium carboxymethyl cellulose, and other suspending agents known to the pharmaceutical formulation art.

[0073] Preferably, the pharmaceutical composition is in unit dosage form. In such form, the composition is divided into unit doses containing appropriate quantities of the active piperidine-3-carboxamide. The unit dosage form can be a

packaged preparation, the package containing discrete quantities of the preparation, for example, packeted tablets, capsules, and powders in vials or ampules. The unit dosage form can also be a capsule, cachet, or tablet itself, or it can be the appropriate number of any of these packaged forms.

[0074] As pharmaceutical compositions for treating infections, pain, or any other indication the compounds of the present invention are generally in a pharmaceutical composition so as to be administered to a subject at dosage levels of from 0.7 to 7000 mg per day, and preferably 1 to 500 mg per day, for a normal human adult of approximately 70 kg of body weight, this translates into a dosage of from 0.01 to 100 mg/kg of body weight per day. The specific dosages employed, however, can be varied depending upon the requirements of the patient, the severity of the condition being treated, and the activity of the compound being employed. The determination of optimum dosages for a particular situation is within the skill of the art.

[0075] Variant piperidine-3-carboxamide derivative compounds and combinatorial libraries can be prepared as shown in figures 1 and 2 in order to achieve a high level of diversity.

[0076] Resins suitable for use in the present invention can easily be determined by one skilled in the art. Such resins include but are not limited to polystyrene resin (e.g. Wang resin : *p*-benzyloxybenzyl alcohol-polystyrene) and PEG-grafted polystyrene resin (e.g. Tentagel, Argogel).

[0077] Other suitable resins known in the art can be found in "Solid Phase Synthesis and Combinatorial Technologies", Seneci, P.; John Wiley and Sons, 2000, p 1-45.

[0078] The resulting compound can be cleaved from the resin. Resin-bound piperidine-3-carboxamide derivative compounds can be cleaved by treating them, for example, with HF. They can also be cleaved with TFA/DCM, provided that TFA sensitive protecting group such as Boc are not used in the synthetic scheme. The compounds can be extracted from the spent resin, for example, with AcOH.

[0079] The nonsupport-bound combinatorial libraries can be screened as

single compounds. In addition, the nonsupport-bound combinatorial libraries can be screened as mixtures in solution in assays such as radio-receptor inhibition assays, anti-bacterial assays, anti-fungal assays, calmodulin-dependent phosphodiesterase (CaMPDE) assays and phosphodiesterase (PDE) assays, as described in detail below. Deconvolution of highly active mixtures can then be carried out by iterative or positional scanning methods. These techniques, the iterative approach or the positional scanning approach, can be utilized for finding other active compounds within the combinatorial libraries of the present invention using any one of the below-described assays or others well known in the art.

[0080] The iterative approach is well-known and is set forth in general in Houghten *et al.*, *Nature*, 354, 84-86 (1991) and Dooley *et al.*, *Science*, 266, 2019-2022 (1994), both of which are incorporated herein by reference. In the iterative approach, for example, sub-libraries of a molecule having three variable groups are made wherein the first variable is defined. Each of the compounds with the defined variable group is reacted with all of the other possibilities at the other two variable groups. These sub-libraries are each tested to define the identity of the second variable in the sub-library having the highest activity in the screen of choice. A new sub-library with the first two variable positions defined is reacted again with all the other possibilities at the remaining undefined variable position. As before, the identity of the third variable position in the sub-library having the highest activity is determined. If more variables exist, this process is repeated for all variables, yielding the compound with each variable contributing to the highest desired activity in the screening process. Promising compounds from this process can then be synthesized on larger scale in traditional single-compound synthetic methods for further biological investigation.

[0081] The positional-scanning approach has been described for various combinatorial libraries as described, for example, in R. Houghten *et al.* PCT/US91/08694 and U.S. Patent 5,556,762, both of which are incorporated herein by reference. In the positional scanning approach, sublibraries are made defining only one variable with each set of sublibraries and all possible sublibraries with each single variable defined (and all other possibilities at all of

the other variable positions), made and tested. From the instant description one skilled in the art could synthesize combinatorial libraries wherein two fixed positions are defined at a time. From the testing of each single-variable defined combinatorial library, the optimum substituent at that position can be determined, pointing to the optimum or at least a series of compounds having a maximum of the desired biological activity. Thus, the number of sublibraries for compounds with a single position defined will be the number of different substituents desired at that position, and the number of all the compounds in each sublibrary will be the product of the number of substituents at each of the other variables.

[0082] Individual compounds and pharmaceutical compositions containing the compounds, as well as methods of using the same, are included within the scope of the present invention. The compounds of the present invention can be used for a variety of purposes and indications and as medicaments for any such purposes and indications. For example, piperidine-3-carboxamide derivative compounds of the present invention can be used as pesticides, acaricides, receptor agonists or antagonists and antimicrobial agents, including antibacterial or antiviral agents. The libraries can be screened in any variety of melanocortin receptor and related activity assays, such as those detailed below as well as others known in the art. Additionally, the subject compounds can be useful as analgesics. Assays which can be used to test the biological activity of the instant compounds include antimicrobial assays, a competitive enzyme-linked immunoabsorbent assay and radio-receptor assays, as described below.

[0083] The melanocortin (MC) receptors are a group of cell surface proteins that mediate a variety of physiological effects, including regulation of adrenal gland function such as production of the glucocorticoids cortisol and aldosterone; control of melanocyte growth and pigment production; thermoregulation; immunomodulation; and analgesia. Five distinct MC receptors have been cloned and are expressed in a variety of tissues, including melanocytes, adrenal cortex, brain, gut, placenta, skeletal muscle, lung, spleen, thymus, bone marrow, pituitary, gonads and adipose tissue (Tatro, Neuroimmunomodulation 3:259-284 (1996)). Three MC receptors, MCR-1, MCR-3 and MCR-4, are expressed in

brain tissue (Xia et al., Neuroreport 6:2193-2196 (1995)).

[0084] A variety of ligands termed melanocortins function as agonists that stimulate the activity of MC receptors. The melanocortins include melanocyte-stimulating hormones (MSH) such as α -MSH, β -MSH and γ -MSH, as well as adrenocorticotropic hormone (ACTH). Individual ligands can bind to multiple MC receptors with differing relative affinities. The variety of ligands and MC receptors with differential tissue-specific expression likely provides the molecular basis for the diverse physiological effects of melanocortins and MC receptors. For example, α -MSH antagonizes the actions of immunological substances such as cytokines and acts to modulate fever, inflammation and immune responses (Catania and Lipton, Annals N. Y. Acad. Sci. 680:412-423 (1993)).

[0085] The role of certain specific MC receptors in some of the physiological effects described above for MC receptors has been elucidated. For example, MCR-1 is involved in pain and inflammation. MCR-1 mRNA is expressed in neutrophils (Catania et al., Peptides 17:675-679 (1996)). The anti-inflammatory agent α -MSH was found to inhibit migration of neutrophils. Thus, the presence of MCR-1 in neutrophils correlates with the anti-inflammatory activity of α -MSH.

[0086] An interesting link of MC receptors to regulation of food intake and obesity has recently been described. The brain MC receptor MCR-4 has been shown to function in the regulation of body weight and food intake. Mice in which MCR-4 has been knocked out exhibit weight gain (Huszar et al., Cell 88:131-141 (1997)). In addition, injection into brain of synthetic peptides that mimic melanocortins and bind to MCR-4 caused suppressed feeding in normal and mutant obese mice (Fan et al., Nature 385:165-168 (1997)). These results indicate that the brain MC receptor MCR-4 functions in regulating food intake and body weight.

[0087] Due to the varied physiological activities of MC receptors, high affinity ligands of MC receptors could be used to exploit the varied physiological responses of MC receptors by functioning as potential therapeutic agents or as lead compounds for the development of therapeutic agents. Furthermore, due to

the effect of MC receptors on the activity of various cytokines, high affinity MC receptor ligands could also be used to regulate cytokine activity.

[0088] A variety of assays can be used to identify or characterize MC receptor ligands of the invention. For example, the ability of a piperidine-3-carboxamide derivative compound to compete for binding of a known MC receptor ligand can be used to assess the affinity and specificity of a piperidine-3-carboxamide derivative compound for one or more MC receptors. Any MC receptor ligand can be used so long as the ligand can be labeled with a detectable moiety. The detectable moiety can be, for example, a radiolabel, fluorescent label or chromophore, or any detectable functional moiety so long as the MC receptor ligand exhibits specific MC receptor binding. A particularly useful detectable MC receptor ligand for identifying and characterizing other MC receptor ligands is 125I-HP 467, which has the amino acid sequence Ac-Nle-Gln-His-(*p*(I)-D-Phe)-Arg-(D-Trp)-Gly-NH₂ and is described in Dooley et al., "Melanocortin Receptor Ligands and Methods of Using Same," U.S. patent application 09/027,108, filed February 20, 1998, which is incorporated herein by reference. HP 467 is a *para*-iodinated form of HP 228.

[0089] Using assay methods such as those described above, binding kinetics and competition with radiolabeled HP 467 can confirm that piperidine-3-carboxamide derivative compounds of the invention bind to one or more MC receptors. Furthermore, piperidine-3-carboxamide derivative compounds of the invention can exhibit a range of affinities and specificity for various MC receptors.

[0090] The invention provides MC receptor ligands that can bind to several MC receptors with similar affinity. In addition, the invention also provides MC receptor ligands that can be selective for one or more MC receptors. As used herein, the term "selective" means that the affinity of a MC receptor ligand differs between one MC receptor and another by about 10-fold, generally about 20- to 50-fold, and particularly about 100-fold. In some cases, a MC receptor ligand having broad specificity is desired. In other cases, it is desirable to use MC receptor ligands having selectivity for a particular MC receptor. For example, MCR-1 ligands are particularly useful for treating pain and inflammation, whereas

MCR-4 ligands are useful for treating obesity. The binding characteristics and specificity of a given MC receptor ligand can be selected based on the particular disease or physiological effect that is desired to be altered.

[0091] Another assay useful for identifying or characterizing MC receptor ligands measures signaling of MC receptors. MC receptors are G protein-coupled receptors that couple to adenylate cyclase and produce cAMP. Therefore, measuring cAMP production in a cell expressing a MC receptor and treated with a MC receptor ligand can be used to assess the function of the MC receptor ligand in activating a MC receptor.

[0092] Ligands for MC-3 that can alter the activity of an MC-3 receptor can be useful for treating sexual dysfunction and other conditions or conditions associated with MC-3 such as inflammation. Other MC-3-associated conditions that can be treated with the MC-3 receptor ligands include disuse deconditioning; organ damage such as organ transplantation or ischemic injury; adverse reactions associated with cancer chemotherapy; diseases such as atherosclerosis that are mediated by free radicals and nitric oxide action; bacterial endotoxic sepsis and related shock; adult respiratory distress syndrome; and autoimmune or other patho-immunogenic diseases or reactions such as allergic reactions or anaphylaxis, rheumatoid arthritis, inflammatory bowel disease, ulcerative colitis, glomerulonephritis, systemic lupus erythematosus, transplant atherosclerosis and parasitic mediated immune dysfunctions such as Chagas's disease.

[0093] The invention further provides a method for treating an MC-3-associated condition in a subject. The term "MC-3-associated condition" includes any condition or condition mediated by MC-3 or can be affected by binding an MC-3 ligand. Such conditions include inflammation and sexual dysfunction.

[0094] The term "sexual dysfunction" herein means any condition that inhibits or impairs normal sexual function, including coitus. However, the term need not be limited to physiological conditions, but may include psychogenic conditions or perceived impairment without a formal diagnosis of pathology.

[0095] In males, sexual dysfunction includes erectile dysfunction. The term "erectile dysfunction" or "impotence" means herein the inability or impaired ability to attain or sustain an erection that would be of satisfactory rigidity for coitus. Sexual dysfunction in males can also include premature ejaculation and priapism, which is a condition of prolonged and sometimes painful erection unrelated to sexual activity, often associated with sickle-cell disease.

[0096] In females, sexual dysfunction includes sexual arousal disorder. The term "sexual arousal disorder" means herein a persistent or recurrent failure to attain or maintain the lubrication-swelling response of sexual excitement until completion of sexual activity. Sexual dysfunction in females can also include inhibited orgasm and dyspareunia, which is painful or difficult coitus. Sexual dysfunction can also be manifested as inhibited sexual desire or inhibited lordosis behavior in animals.

[0097] In addition, the ability of the compounds to inhibit bacterial growth, and therefore be useful to that infection, can be determined by methods well known in the art. Compounds of the present invention can be shown to have antimicrobial activity by the *in vitro* antimicrobial activity assay described below and, therefore, are useful as antimicrobial agents.

[0098] Moreover, an exemplary *in vitro* antimicrobial activity assay is described in Blondelle and Houghten, *Biochemistry* 30:4671-4678 (1991), which is incorporated herein by reference. In brief, *Staphylococcus aureus* ATCC 29213 (Rockville, MD) is grown overnight at 37°C in Mueller-Hinton broth, then re-inoculated and incubated at 37°C to reach the exponential phase of bacterial growth (i.e., a final bacterial suspension containing 10⁵ to 5 x 10⁵ colony-forming units/ml). The concentration of cells is established by plating 100 µl of the culture solution using serial dilutions (e.g., 10-2, 10-3 and 10-4) onto solid agar plates. In 96-well tissue culture plates, compounds, individual or in mixtures, are added to the bacterial suspension at concentrations derived from serial two-fold dilutions ranging from 1500 to 2.9 µg/ml. The plates are incubated overnight at 37°C and the growth determined at each concentration by OD620 nm. The IC₅₀

(the concentration necessary to inhibit 50% of the growth of the bacteria) can then be calculated.

[0099] The competitive ELISA method which can be used here is a modification of the direct ELISA technique described previously in Appel et al., J. Immunol. 144:976-983 (1990), which is incorporated herein by reference. It differs only in the MAb addition step. Briefly, multi-well microplates are coated with the antigenic peptide (Ac-GASPYPNLSNQQT-NH₂) at a concentration of 100 pmol/50 µl. After blocking, 25 µl of a 1.0 mg/ml solution of each mixture of a synthetic combinatorial library (or individual compound) is added, followed by MAb 125-10F3 (Appel et al., *supra*) (25 µl per well). The MAb is added at a fixed dilution in which the bicyclic guanidine in solution effectively competes for MAb binding with the antigenic peptide adsorbed to the plate. The remaining steps are the same as for direct ELISA. The concentration of compound necessary to inhibit 50% of the MAb binding to the control peptide on the plate (IC₅₀) is determined by serial dilutions of the compound.

[0100] Alternative screening can be done with radio-receptor assays. The radio-receptor assay, can be selective for any one of the μ , κ , or δ opiate receptors. Compounds of the present invention can be useful *in vitro* for the diagnosis of relevant opioid receptor subtypes, such as κ , in the brain and other tissue samples. Similarly, the compounds can be used *in vivo* diagnostically to localize opioid receptor subtypes.

[0101] The radio-receptor assays are also an indication of the compounds' analgesic properties as described, for example, in Dooley et al., *Proc. Natl. Acad. Sci.*, 90:10811-10815 (1993). For example, it can be envisioned that these compounds can be used for therapeutic purposes to block the peripheral effects of a centrally acting pain killer. For instance, morphine is a centrally acting pain killer. Morphine, however, has a number of deleterious effects in the periphery which are not required for the desired analgesic effects, such as constipation and pruritus (itching). While it is known that the many compounds do not readily cross the blood-brain barrier and, therefore, elicit no central effect, the subject

compounds can have value in blocking the periphery effects of morphine, such as constipation and pruritus. Accordingly, the subject compounds can also be useful as drugs, namely as analgesics, or to treat pathologies associated with other compounds which interact with the opioid receptor system.

[0102] Additionally, such compounds can be tested in a σ receptor assay. Ligands for the σ receptor can be useful as antipsychotic agents, as described in Abou-Gharbia et al., *Annual Reports in Medicinal Chemistry*, 28:1-10 (1993).

[0103] Radio-receptor assays can be performed with particulate membranes prepared using a modification of the method described in Pasternak et al., *Mol. Pharmacol.* 11:340-351 (1975), which is incorporated herein by reference. Rat brains frozen in liquid nitrogen can be obtained from Rockland (Gilbertsville, PA). The brains are thawed, the cerebella removed and the remaining tissue weighed. Each brain is individually homogenized in 40 ml Tris-HCl buffer (50 mM, pH 7.4, 4°C) and centrifuged (Sorvall® RC5C SA-600: Du Pont, Wilmington, DE) (16,000 rpm) for 10 minutes. The pellets are resuspended in fresh Tris-HCl buffer and incubated at 37°C for 40 minutes. Following incubation, the suspensions are centrifuged as before, the resulting pellets resuspended in 100 volumes of Tris buffer and the suspensions combined. Membrane suspensions are prepared and used in the same day. Protein content of the crude homogenates generally range from 0.15-0.2 mg/ml as determined using the method described in Bradford, M.M., *Anal. Biochem.* 72:248-254 (1976), which is incorporated herein by reference.

[0104] Binding assays are carried out in polypropylene tubes, each tube containing 0.5 ml of membrane suspension. 8 nM of 3H-[D-Ala₂,Me-Phe₄,Gly-ol₅]enkephalin (DAMGO) (specific activity = 36 Ci/mmol, 160,000 cpm per tube; which can be obtained from Multiple Peptide Systems, San Diego, CA, through NIDA drug distribution program 271-90-7302) and 80 μ g/ml of bicyclic guanidine, individual or as a mixture and Tris-HCl buffer in a total volume of 0.65 ml. Assay tubes are incubated for 60 mins. at 25°C. The reaction is terminated by filtration through GF-B filters on a Tomtec harvester (Orange, CT). The filters are

subsequently washed with 6 ml of Tris-HCl buffer, 4°C. Bound radioactivity is counted on a Pharmacia Biotech Betaplate Liquid Scintillation Counter (Piscataway, NJ) and expressed in cpm. To determine inter- and intra-assay variation, standard curves in which 3H-DAMGO is incubated in the presence of a range of concentrations of unlabeled DAMGO (0.13-3900 nM) are generally included in each plate of each assay (a 96-well format). Competitive inhibition assays are performed as above using serial dilutions of the piperidine-3-carboxamides, individually or in mixtures. IC₅₀ values (the concentration necessary to inhibit 50% of 3H-DAMGO binding) are then calculated. IC₅₀ values of less than 1000 nM are indicative of highly active opioid compounds which bind to the μ receptor, with particularly active compounds having IC₅₀ values of 100 nM or less and the most active compounds with values of less than 10 nM.

[0105] As opposed to this μ receptor selective assay, which can be carried out using 3H-DAMGO as radioligand, as described above, assays selective for κ receptors can be carried out using [3H]-U69,593 (3 nM, specific activity 62 Ci/mmol) as radioligand. Assays selective for δ opiate receptors can be carried out using tritiated DSLET ([D-Ser₂, D-Leu₅]-threonine-enkephalin) as radioligand. Assays selective for the σ opiate receptor can use radiolabeled pentazocine as ligand.

[0106] Screening of combinatorial libraries and compounds of the invention can be done with an anti-fungal assay. Compounds of the present invention can be useful for treating fungal infections.

[0107] Screening of combinatorial libraries and compounds of the invention also can be done with a calmodulin-dependent phosphodiesterase (CaMPDE) assay. Compounds of the present invention can be useful as calmodulin antagonists.

[0108] Calmodulin (CaM), which is the major intracellular calcium receptor, is involved in many processes that are crucial to cellular viability. In particular, calmodulin is implicated in calcium-stimulated cell proliferation. Calmodulin

antagonists are, therefore, useful for treating conditions associated with increased cell proliferation, for example, cancer. In addition, calmodulin antagonists such as compounds of the subject invention are useful both in vitro and in vivo for identifying the role of calmodulin in other biological processes. The disadvantages of known antagonists such as trifluoperazine and N-(4-aminobutyl)-5-chloro-2-naphthalenesulfonamide (W13) include their non-specificity and toxicity. In contrast, advantages of the combinatorial libraries and compounds of the subject invention as calmodulin antagonists include their reduced flexibility and ability to generate broader conformational space of interactive residues as compared to their linear counterparts.

[0109] An example of an assay that identifies CaM antagonists is a CaMPDE assay. In brief, samples are mixed with 50 μ l of assay buffer (360 mM Tris, 360 mM Imidazole, 45 mM Mg(CH₃COO)₂, pH 7.5) and 10 μ l of CaCl₂ (4.5 mM) to a final volume of 251 μ l. 25 μ l of calmodulin stock solution (Boehringer Mannheim; 0.01 μ g/ μ l) is then added and the samples then sit at room temperature for 10 minutes. 14 μ l of PDE (Sigma; 2 Units dissolved in 4 ml of water; stock concentration: 0.0005 Units/ μ l) is then added, followed by 50 μ l of 5'-nucleotidase (Sigma; 100 Units dissolved in 10 ml of 10 mM Tris-HCl containing 0.5 mM Mg(CH₃COO)₂, pH 7.0; stock concentration: 10 Units/ml). The samples are then incubated for 10 minutes at 30°C. 50 μ l of adenosine 3',5'-cyclic monophosphate (cAMP) (20 mM in water at pH 7.0) is added, the samples incubated for 1 hour at 30°C and then vortexed. 200 μ l of trichloroacetic acid (TCA) (55% in water) is added to a 200 μ l sample aliquot, which is then vortexed and centrifuged for 10 minutes. 80 μ l of the resulting supernatants of each sample is transferred to a 96-well plate, with 2 wells each containing 80 μ l of each sample. 80 μ l of ammonium molybdate (1.1% in 1.1N H₂SO₄) is then added to all the wells, and the OD of each were determined at 730nm, with the values later subtracted to the final OD reading. 16 μ l of reducing agent (6g sodium bisulfite, 0.6g sodium sulfite and 125mg of 1-amino-2-naphtol-4-sulfonic acid in 50ml of water) is then added to one of each sample duplicate and 16 μ l of water is added to the other duplicate. After sitting for 1 hour at room

temperature, the OD of each well is determined at 730nm. The percent inhibition of calmodulin activity is then calculated for each sample, using as 0% inhibition a control sample containing all reagents without any test samples and as 100% inhibition a control sample containing test samples and all reagents except calmodulin. In addition, the percent inhibition of phosphodiesterase activity was determined by following a similar protocol as the CaMPDE assay described above, except not adding calmodulin to the sample mixture and calculating the percent inhibition by using as 0% inhibition a control reagent without any test samples and as 100% inhibition a control sample containing test samples and all reagents except cAMP.

[0110] The following examples are provided to illustrate but not limit the present invention. The following abbreviations have the corresponding meanings:

- DMF : N,N-dimethylformamide;
HOBr : 1-hydroxybenzotriazole;
Boc : tert-butoxycarbonyl;
DIC : N,N-diisopropylcarbodiimide;
TFA : trifluoroacetic acid;
DIEA : N,N-diisopropylethylamine;
DCM : dichloromethane;
RT : room temperature
MeOH: methanol
MeOEtOH : 2-methoxyethanol
DCE : 1,2-dichloroethane
THF : tetrahydrofuran
ACN : acetonitrile
Wang resin : *p*-benzyloxybenzyl alcohol-polystyrene Br-Wang resin :
p-benzyloxybenzyl bromide-polystyrene
PP : polypropylene
PPh₃Br₂ : triphenylphosphine dibromide
DMAP : 4-dimethylamino-pyridine

Example 1
Synthetic Protocol

Step 1a. Loading Hydroxybenzaldehydes on Bromo-Wang Resin

[0111] A 1 L Pyrex media bottle was charged with 100 g Bromo-Wang resin (100-200 mesh, 1.4 mmol/g). DMF (350 ml) was added and the bottle was shaken by hand to distribute the solvent within the swollen resin. A 500 ml Pyrex media bottle was charged with the hydroxybenzaldehyde (420 mmol, 3 eq) and the aldehyde was dissolved in DMF (300 ml). The aldehyde solution was cooled to 0° C (ice bath) and potassium *tert*-butoxide (44.8 g, 400 mmol) was added in two equal portions shaking for about 5 min. between additions. CAUTION: EXOTHERMIC REACTION. The temperature must be maintained at or below 25° C. The bottle was removed from the ice bath and shaken periodically to help dissolve the potassium *tert*-butoxide completely. After the second portion of potassium *tert*-butoxide was added, the bottle was allowed to warm to 25° C. After 30 min. at 25° C, all the potassium *tert*-butoxide dissolved and the solutions had various dark colors. The phenoxide solution was added to the swollen resin in two portions, shaking between portions. The 1L bottles were clamped horizontally in an orbital shaker oven and allowed to shake at 25° C for 30 min. The temperature was then increased to 50° C and the reaction allowed to shake for 14 h. After cooling, each resin slurry was poured into a 8" x 10" 3-sided porous polypropylene packet (tea bag) sitting in a 2 L beaker. After the solvent mixture had drained from the resin, the fourth side of the tea bag was sealed and the tea bags were washed in wide-mouth HDPE Nalgene bottles as follows: 2 x DMF, 4 x DMF/H₂O (4:1), 3 x DMF, 4 x MeOH. The tea bags were allowed to air dry in a fume hood.

Step 1b. Loading Diamines on Wang-Imidazolide Resin

[0112] For each R₁ diamine, a 4 L Nalgene bottle was charged with 17 x 2.5 g

tea bags containing Wang resin (100-200 mesh, 1.4 mmol/g). DCM (2 L) was added followed by 1,1'-carbonyldiimidazole (97 g, 0.60 mol, 0.3 M). The bags were shaken for 3 h at room temperature. Each diamine (0.72 mol, 0.4 M) was placed in a 2 L Nalgene bottle and 1.8 L of DCM added.

[0113] After 3 h shaking with CDI, the Wang-imidazolide tea bags were washed quickly with DCM (x2). The diamine solution was added immediately and the bags shaken overnight at room temperature. The bags were washed with DCM (x3) and MeOH (x3).

Step 2a. Imine Formation for the R₁ Hydroxybenzaldehydes.

[0114] After splitting the tea bags from step 1a, each set of 8 x 2.5 g bags was placed into a 1 L Nalgene bottle. The containers were then filled with 250 ml of trimethylorthoformate and 250 ml of anhydrous DMF. After the bags were saturated with the solvent, the primary amine (150 mmol, 0.3 M) was added. The reaction was then allowed to shake at room temperature for 24 h. The wash procedure must be carried out just before step 3 and the description is included in that section.

Step 2b. Imine Formation for the R₁ Primary Diamines.

[0115] After splitting the tea bags from step 1b, each set of 7 x 2.5 g bags was placed into a 1 L Nalgene bottle. The containers were then filled with 250 ml of trimethylorthoformate and 250 ml of anhydrous DMF. After the bags were saturated with the solvent, the aldehyde (150 mmol, 0.3 M) was added. The reaction was then shaken at room temperature for 24 h. The wash procedure must be carried out just before step 3 and is described in that section.

Step 3. Cyclization with 2-Phenylglutaric Anhydride

[0116] In an 8L Nalgene bottle, 2-Phenylglutaric anhydride (1.0 mol, 0.4M) was completely dissolved in 2.5L anhydrous DMF and triethylamine (0.03 M) was added. This anhydride solution is created before washing the imine tea bags. The imine tea bags from step 2 (60 X 2.5g bags) were quickly washed with

anhydrous DMF (3 x, 3 minutes or less washing). After washing, the imine bags were immediately transferred to the 2-Phenylglutaric anhydride solution and the reaction shaken at RT for 5 days. The bags were washed with DMF (x3) DCM (x3) and MeOH (x3) and air-dried.

Step 4. Acylation of the Resin Bound Carboxylic Acid.

[0117] Each tea bag from step 3 was plated into 40 wells of a 2 ml deep-well microtiter plate. The resin bound carboxylic acid was pre-activated by treatment with 0.6 ml of a solution containing 0.6 M DIC, 0.6M HOBt in anhydrous DMF. The plates were allowed to stand for one hour at room temperature. During this time, each amine solution was prepared by dissolving the amine (0.6M) in a solution of DIEA (0.8 M) in DMF. To each well containing the pre-activated acid resin was added 0.6 ml of the amine solution. The final concentrations in each well were: amine (0.3M), DIEA (0.4 M), HOBt (0.3 M), and DIC (0.3 M). The plates were vortexed and were placed in a shaker oven at 50° C for 24 h. After cooling to room temperature, the resin was washed using a robotic wash station with 20% water/DMF (x2), DMF (x8) and MeOH (x6) and air-dried.

Step 5. Cleavage from Linker and Extraction

[0118] To dry microtiter plates was added 0.5 ml of 20% TFA/DCM to each well. The plates were capped and placed on a shaker at room temperature for 2 h. The plates were transferred to a GENEVAC to remove the volatile TFA/DCM solution. The resin was extracted with AcOH and the extracts were frozen and lyophilized to afford the products as yellow oils. All of the final products were analyzed by HPLC/MS using ELSD detection to determine purity.

Example 2

Preparation of (Substituted Phenyl)-glutaric anhydrides

[0119] The appropriate substituted phenylacetic acid ethyl or methyl ester **1** (0.01 mol) is dissolved in anhydrous ethanol (100 ml). To this solution is added

Sodium ethoxide (0.01 mol), followed by ethyl acrylate (0.015 mol), and the solution is heated to reflux overnight. The solution is cooled and the solvent evaporated under reduced pressure. The product **2** is then dissolved in 100 ml H₂O/EtOH 1:1 and KOH added (0.10 mol). The solution is heated to reflux for 10 hours, acidified to pH 3 with 1 N HCl and the diacid product **3** extracted with EtOAc, washed with water and brine, and dried with MgSO₄. After removal of the solvent, the resulting solid is suspended in Acetic anhydride (100 ml) and heated to reflux for 1 hour to afford the anhydride. The solvent is removed and the residue is suspended in toluene and evaporated to afford the product **4**.

List of Compounds **1**:

ETHYL 2-THIOPHENEACETATE
ETHYL THIOPHENE-3-ACETATE
INDOLE-3-ACETIC ACID ETHYL ESTER
ETHYL 2-PYRIDYLACETATE
ETHYL 3-PYRIDYLACETATE
ETHYL O-TOLYLACETATE
ETHYL P-TOLYLACETATE
METHYL 1-METHYL-2-PYRROLEACETATE
METHYL 2,3,4,5,6-PENTAFLUOROPHENYLACETATE
ETHYL 2-NAPHTHYLACETATE
METHYL 2-(4,5-DIMETHOXY-2-NITROPHENYL)ACETATE
ETHYL P-BROMOPHENYLACETATE
ETHYL 4-NITROPHENYLACETATE
METHYL 2,3,4-TRIMETHOXYPHENYL ACETATE
METHYL 3,4,5-TRIMETHOXYPHENYL ACETATE
ETHYL 3,4-DIMETHOXYPHENYLACETATE
ETHYL M-TOLYLACETATE
2,4-DICHLOROPHENYLACETIC ACID METHYL ESTER
ETHYL 4-CHLOROPHENYLACETATE
ETHYL 1-NAPHTHYLACETATE
ETHYL 3-METHOXYPHENYLACETATE
ETHYL 4-BENZOLOXYPHENYLACETATE
ETHYL 4-METHOXYPHENYLACETATE
5-BENZOLOXYINDOLE-3-ACETIC ACID METHYL ESTER
ETHYL PYRIDINE-4-ACETATE
METHYL 4-TERT-BUTYLPHENYLACETATE
ETHYL MESITYLACETATE
ETHYL 4-ETHOXYPHENYLACETATE
ETHYL 2-BROMOPHENYLACETATE
4-BUTOXYPHENYLACETIC ACID METHYL ESTER

ETHYL 3,5-DIMETHYLPHENYLACETATE
METHYL 3,5-DIMETHOXYPHENYLACETATE
ETHYL 2-NITROPHENYLACETATE
2-CHLOROPHENYLACETIC ACID METHYL ESTER
METHYL 4-BENZYLOXYPHENYLACETATE
METHYL 5-CHLOROBENZO[B]THIEN-3-YLACETATE
2,6-DICHLOROPHENYLACETIC ACID METHYL ESTER
ETHYL 2,5-DIMETHOXYPHENYLACETATE
METHYL (5-METHYL-2-PHENYLOXAZOL-4-YL)ACETATE
METHYL 5,6-DICHLORO-3-INDOLEACETATE
METHYL 2-(5-METHOXY-2-METHYL-1H-INDOL-3-YL)ACETATE
METHYL (5-METHYL-2-PHENYLTHIAZOL-4-YL)ACETATE
IMIDAZO(2,1-B)THIAZOL-6-YL-ACETIC ACID ETHYL ESTER
(4-CHLORO-2-NITRO-PHENYL)-ACETIC ACID ETHYL ESTER
ETHYL 2-(TRIFLUOROMETHYL)PHENYL ACETATE
ETHYL 2-[2-(ACETYLAMINO)-1,3-THIAZOL-4-YL]ACETATE
(1H-IMIDAZOL-4-YL)-ACETIC ACID METHYL ESTER
(4,5-DIMETHOXY-2-NITRO-PHENYL)-ACETIC ACID ETHYL ESTER
ETHYLFURYL ACETATE
METHYL 2-FLUOROPHENYLACETATE
METHYL 2-CHLORO-6-FLUOROPHENYLACETATE
METHYL 4-FLUOROPHENYLACETATE
METHYL 2-CHLORO-4-FLUOROPHENYL ACETATE
METHYL 3-CHLOROPHENYLACETATE
METHYL 3,4-DICHLOROPHENYLACETATE
ETHYL 2-(2-PHENYL-1,3-THIAZOL-4-YL)ACETATE
ETHYL 3,4-DICHLOROPHENYLACETATE
ETHYL 2-(2-METHYL-1,3-THIAZOL-4-YL)ACETATE
ETHYL 2-[2-[4-(TERT-BUTYL)PHENYL]-1,3-THIAZOL-4-YL]ACETATE
ETHYL 2-[2-(4-CHLOROPHENYL)-1,3-THIAZOL-4-YL]ACETATE
METHYL (2-CYANOPHENYL)ACETATE
METHYL (4-CYANOPHENYL)ACETATE

Example 3

Anti-microbial Screen

[0120] *Streptococcus pyogenes* (ATCC# 97-03 14289) was grown in Todd Hewitt Broth (THB) (Difco Laboratories #0492-17-6) overnight until reaching an optical density of (OD = 0.636@ 570 nm) by reading 0.1 ml in a 96 well microtiter plate in a Molecular Devices Thermomax. This preparation was kept frozen as stocks in 30% v/v glycerol in 1.5 ml aliquots at -70mC until use. Prior to experiments, 6 ml aliquots were thawed and diluted into 50 ml 2X THB. 60 ul

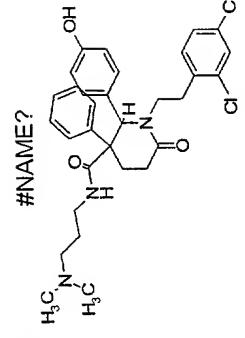
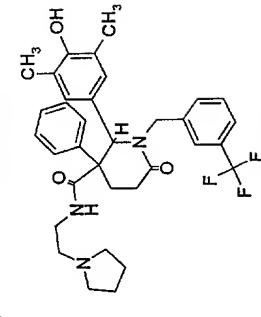
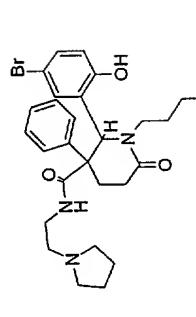
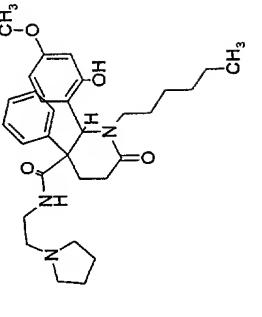
of this dilution was added to 92 wells of microtiter plate. To three wells THB (200 ul) was added to serve as a blank and a sterility control. Test compounds in DMSO and appropriate concentrations of DMSO were added to Growth/Solvent Controls at 0 time. Plates were read at 0 time at 570 nm in the Molecular Devices plate reader to obtain compounds correction factors for insoluble or colored compounds. Plates were read again at 4 hours.

[0121] Percent inhibition is calculated with the following formula

[0122] Color correct = O.D. 0 hr - Blank 0 hr)-(Solvent Control 0hr - Blank 0 hr)

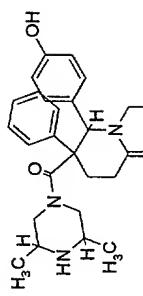
[0123] % Inhibition =

$$100 - \frac{\text{O.D. test compound 4 hr} - \text{Blank 4 hr} - \text{color correct}}{\text{O.D. growth/solvent control 4 hr} - \text{Blank 4 hr}}$$

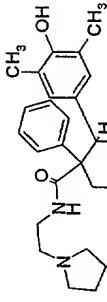
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9100	682	1	000726065	9100-009	B 07	0.112	98.90	Spy4H	0.1776	TR0910000682		#NAME? C ₃₄ H ₃₈ F ₃ N ₃ O ₃ 593.686
9100	2442	1	000727585	9100-035	B 07	0.17	97.52	Spy4H	0.1776	TR0910002442		#NAME? C ₃₀ H ₄₀ Br N ₃ O ₃ 570.568
9100	3002	1	000728145	9100-042	B 07	0.112	97.51	Spy4H	0.1776	TR0910003002		#NAME? C ₃₁ H ₄₃ N ₃ O ₄ 521.698

Library	Compound ID	Expt Reg.	Plate	Well	Raw Data	Assay Result	Assay Concentration/mM	LionID	
9100	2989	1	000728132	9100-042	E 05	0.203	97.24	Spy4H	0.1776 TR0910002989
9100	2482	1	000727625	9100-036	B 02	0.13	96.59	Spy4H	0.1776 TR0910002482
9100	2509	1	000727652	9100-036	E 05	0.162	96.33	Spy4H	0.1776 TR0910002509
9100	669	1	000726052	9100-009	E 05	0.207	96.21	Spy4H	0.1776 TR0910000669

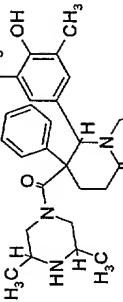
#NAME? C₃₂H₃₅Cl₂N₃O₃ 580.552



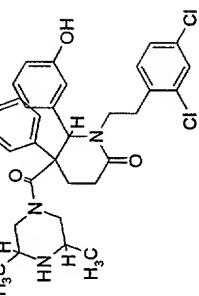
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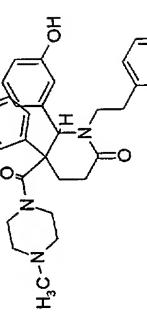
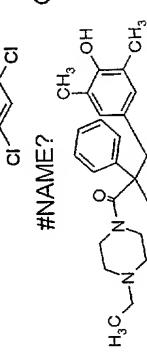
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#NAME? C₃₄H₃₉Cl₂N₃O₃ 608.606



Library	Compound Lot	ExReg	Plate	Well	Raw Data	Assay Result	Assay	Conc ng/ml	LionID	
9100	3739	1	000728882	9100-051	C 09	0.132	94.27	Spy4H	0.1776	TR0910003739
9100	1029	1	000726412	9100-013	E 10	0.162	94.11	Spy4H	0.1776	TR0910001029
9100	2402	1	000727545	9100-035	B 02	0.12	92.38	Spy4H	0.1776	TR0910002402
								#NAME?		491.672
								#NAME?		525.689
								#NAME?		570.73

Library	Cmpd ID	Expt Req.	Plate	Well	Raw Data	Assay	Result	Assay Concentration	LionID	#NAME?	
9100	2469	1	000727612	9100-035 E 10	0.231	90.14	Spy4H	0.1776	TR0910002469	C ₃₀ H ₄₀ Br N ₃ O ₃	570.568
9100	649	1	000726032	9100-009 A 03	0.217	84.40	Spy4H	0.1776	TR0910000649	#NAME?	566.526
											
9100	2420	1	000727563	9100-035 D 04	0.219	84.37	Spy4H	0.1776	TR0910002420	#NAME?	525.689
											

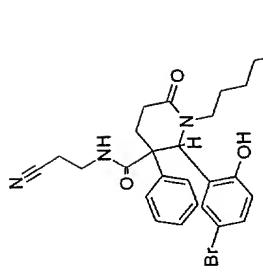
9100 2474 1 000727617 9100-035 B 11 0.265 84.05 Spy4H 0.1776 TR0910002474

Library Cmpd 1st ExReg Plate Well Raw Data Assay Result Conc mg/ml LionID

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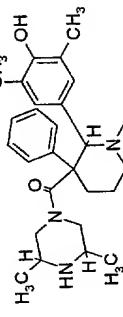
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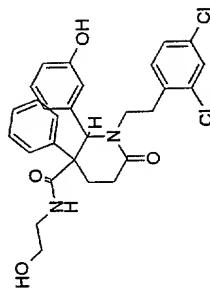
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#NAME? C₃₄H₃₈F₃N₃O₃



9100 657 1 000726040 9100-009 A 04 0.188 83.39 Spy4H 0.1776 TR0910000657

#NAME? C₂₈H₂₈Cl₂N₂O₄



593.686

#NAME?

527.445

Library	Compound ID	ExReg	Plate	Well	Raw Data	Assay Result	Assay	Conc ng/ml	LionID	#NAME?	Chemical Structure	Category	
9100	2602	1	000727745	9100-037	B07	0.157	83.27	Spy4H	0.1776	TR0910002602	C ₃₃ H ₃₈ ClN ₃ O ₃	560.134	
9100	853	1	000726236	9100-011	E08	0.28	83.27	Spy4H	0.1776	TR0910000853	#NAME?	C ₃₂ H ₂₈ ClF N ₂ O ₃	543.035
9100	862	1	000726245	9100-011	F09	0.255	83.27	Spy4H	0.1776	TR0910000862	#NAME?	C ₃₀ H ₃₃ ClN ₂ O ₄	521.054
9100	2444	1	000727587	9100-035	D07	0.275	82.77	Spy4H	0.1776	TR0910002444	#NAME?	C ₂₉ H ₃₅ BrN ₄ O ₃	567.524

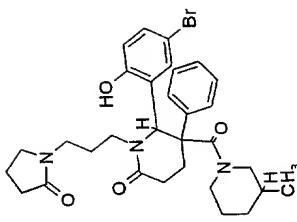
9100 995 1 000726378 9100-013 C 06 0.291

Library Cmpd 1st ExtReg Plate Well Raw Date Assay Result Assay Consing/mi LionID

9100 82.45 Spy4H 0.1776 TR0910000995

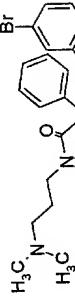
#NAME? C₃₁ H₃₈ Br N₃ O₄ 596.562

#NAME?



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C₂₇ H₃₆ Br N₃ O₃ 530.503



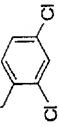
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C₂₆ H₂₄ Cl₂ N₂ O₄ 499.392

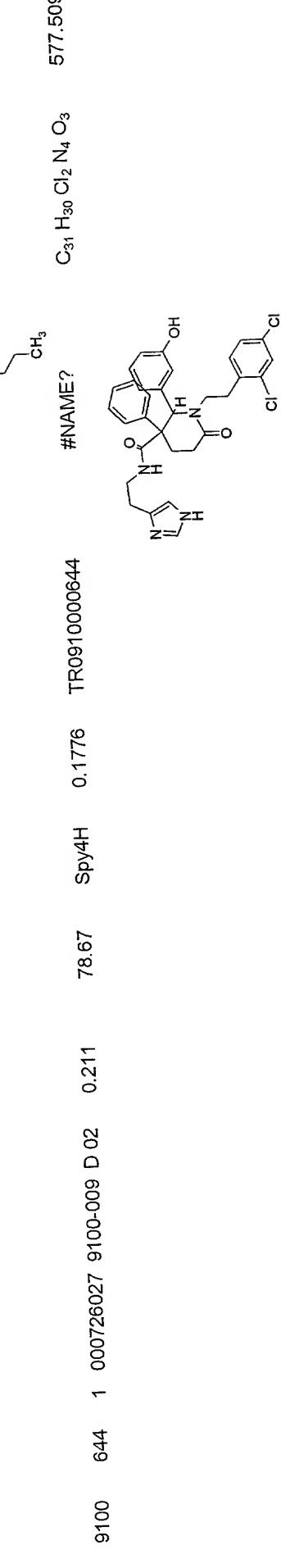
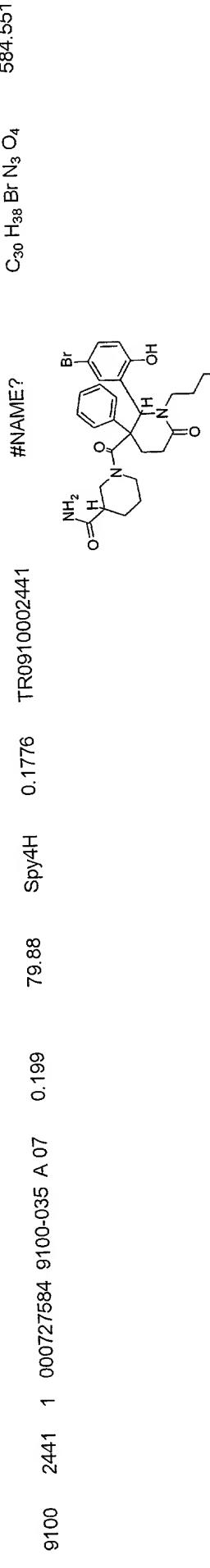
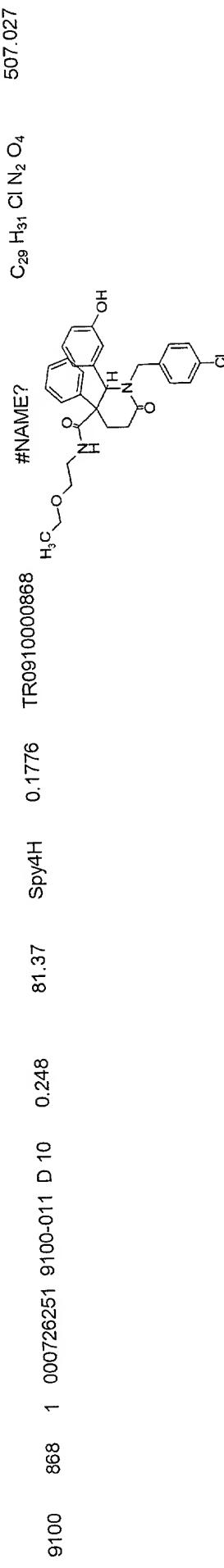
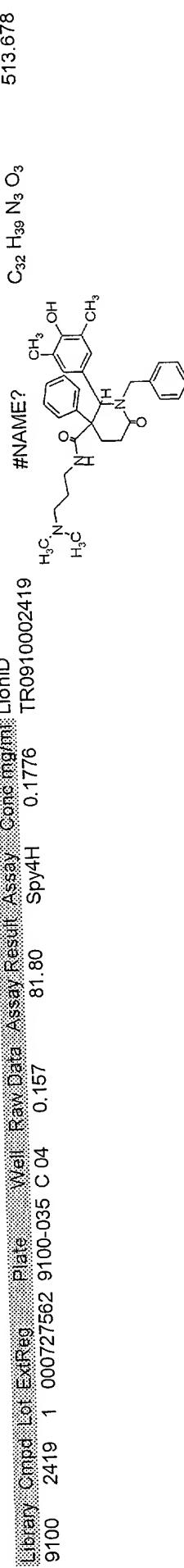


9100 668 1 000726051 9100-009 D 05 0.328 82.04 Spy4H 0.1776 TR0910000668 #NAME?

C₃₀ H₃₂ Cl₂ N₂ O₄ 555.499



9100 2419 1 000727562 9100-035 C 04 0.157 81.80 Spy4H 0.1776 TR0910002419

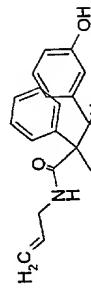


9100 846 1 000726229 9100-011 F 07 0.31

Library Comp Lot ExReg Plate Well Raw Data Assay Result Assay Concentration LionID

9100 846 1 000726229 9100-011 F 07 0.31

474.985



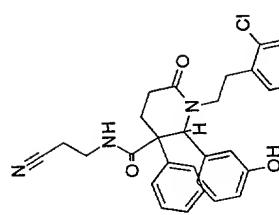
542.514

C₂₈H₂₇ClN₂O₃

9100 674 1 000726057 9100-009 B 06 0.275

Spy4H 0.1776 TR0910000674

#NAME?



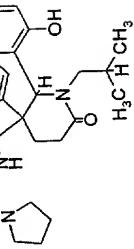
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C₂₉H₂₇Cl₂N₃O₃

9100 1682 1 000726825 9100-023 B 02 0.193

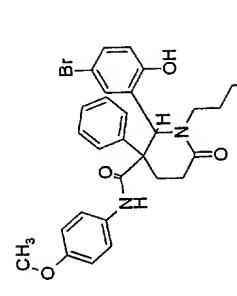
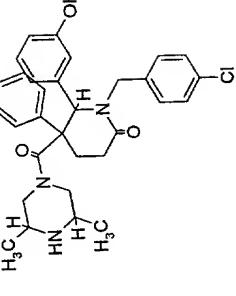
Spy4H 0.1776 TR0910001682

#NAME?



542.514

C₂₈H₃₆BrN₃O₃

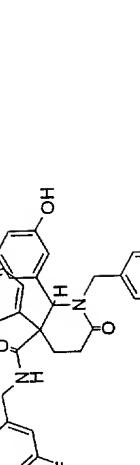
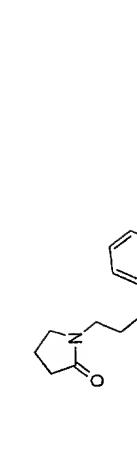
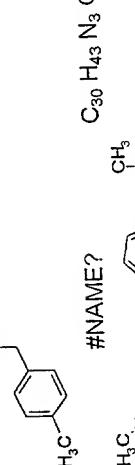
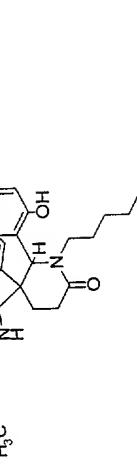
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9100	870	1	000726253	9100-011	F 10	0.278	76.50	Spy4H	0.1776	TR0910000870	C ₂₈ H ₂₅ ClN ₂ O ₃	472.97	
9100	2476	1	000727619	9100-035	D 11	0.35	75.71	Spy4H	0.1776	TR0910002476	#NAME?		579.531
9100	869	1	000726252	9100-011	E 10	0.255	75.69	Spy4H	0.1776	TR0910000869	#NAME?		532.081

Library	Comp	Lot	ExReg	Plate	Well	Raw Data	Assay	Conc/mM	LionID	#NAME?	
9100	677	1	000726060	9100-009	E 06	0.23	75.63	Spy4H	0.1776	TR0910000677	C ₂₆ H ₂₄ Cl ₂ N ₂ O ₄
9100	1006	1	000726389	9100-013	F 07	0.334	75.14	Spy4H	0.1776	TR0910001006	#NAME?
9100	1101	1	000726484	9100-014	E 09	0.263	74.29	Spy4H	0.1776	TR0910001101	#NAME?
9100	1003	1	000726386	9100-013	C 07	0.302	74.05	Spy4H	0.1776	TR0910001003	#NAME?
											448.603
											422.566
											434.577
											499.392

Library CompID ExReg Plate Well Raw Data Assay Result Concentration IonID

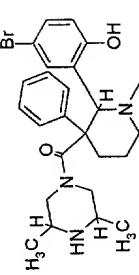
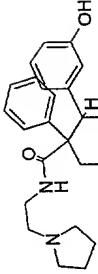
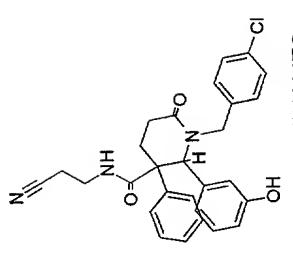
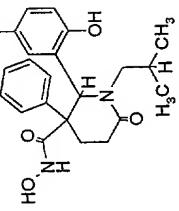
Library CompID	ExReg	Plate	Well	Raw Data	Assay	Result	Concentration	IonID				
9100	859	1	000726242	9100-011 C 09	0.204	73.80	Spy4H	0.1776	TR0910000859	#NAME?	C ₃₀ H ₃₄ ClN ₃ O ₃	520.07
9100	2409	1	000727552	9100-035 A 03	0.211	73.79	Spy4H	0.1776	TR0910002409	#NAME?	C ₃₂ H ₃₇ N ₃ O ₃	511.662
9100	2450	1	000727593	9100-035 B 08	0.294	73.79	Spy4H	0.1776	TR0910002450	#NAME?	C ₂₉ H ₃₇ BrN ₂ O ₄	557.525

Library	Compound ID	ExReg	Plate	Well	Raw Data	Assay	Result	Assay	Conc mg/ml	LionID		
9100	2462	1	000727605	9100-035 F 09	0.254	73.79	Spy4H	0.1776	TR0910002462	#NAME?	C ₂₈ H ₃₉ BrN ₂ O ₄	559.541
9100	1716	1	000726859	9100-023 D 06	0.445	73.16	Spy4H	0.1776	TR0910001716	#NAME?	C ₂₉ H ₃₁ BrN ₂ O ₄	551.478
9100	858	1	000726241	9100-011 B 09	0.303	72.99	Spy4H	0.1776	TR0910000858	#NAME?	C ₃₀ H ₂₇ ClN ₂ O ₃ S	531.073
9100	1030	1	000726413	9100-013 F 10	0.28	72.97	Spy4H	0.1776	TR0910001030	#NAME?	C ₂₇ H ₃₂ N ₂ O ₃	432.561

LionID	Compound ID	Lot	Ex Reg.	Plate	Well	Raw Date	Assay Result	Assay	Conc mg/ml	LionID	#NAME?	Chemical Structure
9100	852	1	000726235	9100-011	D 08	0.332	72.45	Spy4H	0.1776	TR0910000852	C ₃₂ H ₂₈ ClF N ₂ O ₃	
9100	3731	1	000728874	9100-051	C 08	0.3	72.29	Spy4H	0.1776	TR0910003731	#NAME?	
9100	3019	1	000728162	9100-042	C 09	0.205	72.18	Spy4H	0.1776	TR0910003019	#NAME?	
9100											C ₃₀ H ₄₃ N ₃ O ₄	
											509.687	

三

LibID	Cmpd Lot	E Reg#	Plate	Well	Raw Data	Assay Result	Assay	Conc ng/ml	LionID	#NAME?	
9100	860	1	000726243	9100-011 D 09	0.266	72.18	Spy4H	0.1776	TR0910000860	C ₃₁ H ₃₄ Cl N ₃ O ₃	532.081
9100	1708	1	000726851	9100-023 D 05	0.379	72.09	Spy4H	0.1776	TR0910001708	H ₃ C #NAME?	517.461
9100	2468	1	000727611	9100-035 D 10	0.28	71.54	Spy4H	0.1776	TR0910002468	H ₃ C #NAME?	545.514
9100	2733	1	000727876	9100-039 E 03	0.429	71.19	Spy4H	0.1776	TR0910002733	F CH ₃ #NAME?	573.061

Library	Cmpd Loci	ExReg	Plate	Well	Raw Data	Assay Ref#	Assay	Conc ng/ml	LionID		
9100	1709	1	000726852	9100-023	E 05	0.383	71.02	Spy4H	0.1776	TR0910001709	#NAME?
											
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											#NAME?
9100	842	1	000726225	9100-011	B 07	0.215	70.82	Spy4H	0.1776	TR0910000842	#NAME?
											
											<chem>CC(C)C[C@H]1[C@@H]2[C@H]3[C@H]1O[C@H]2[C@H]4[C@H]3[C@H]4Cc5ccc(Cl)cc5</chem>
											#NAME?
9100	874	1	000726257	9100-011	B 11	0.256	70.82	Spy4H	0.1776	TR0910000874	#NAME?
											
											<chem>CC(C)C[C@H]1[C@@H]2[C@H]3[C@H]1O[C@H]2[C@H]4[C@H]3[C@H]4Cc5ccc(Cl)cc5</chem>
											#NAME?
9100	1717	1	000726860	9100-023	E 06	0.329	70.21	Spy4H	0.1776	TR0910001717	#NAME?
											
											<chem>CC(C)C[C@H]1[C@@H]2[C@H]3[C@H]1O[C@H]2[C@H]4[C@H]3[C@H]4Cc5ccc(Br)cc5</chem>
											#NAME?
											<chem>CC(C)C[C@H]1[C@@H]2[C@H]3[C@H]1O[C@H]2[C@H]4[C@H]3[C@H]4Cc5ccc(Br)cc5</chem>
											C ₂₈ H ₃₆ BrN ₃ O ₃
											542.514
											C ₂₈ H ₃₆ ClN ₃ O ₃
											532.081
											C ₃₁ H ₃₄ ClN ₃ O ₃
											487.984
											C ₂₈ H ₂₆ ClN ₃ O ₃
											461.353
											C ₂₂ H ₂₅ BrN ₂ O ₄
											461.353

Library	Compound ID	Lot	Expt #	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1093	1	000726476	9100-014	E 08	0.307	70.04	Spy4H	0.1776	TR0910001093	#NAME?	C ₂₈ H ₂₉ F N ₂ O ₃	460.546
9100	844	1	000726227	9100-011	D 07	0.221	69.74	Spy4H	0.1776	TR0910000844	#NAME?	C ₃₀ H ₂₉ Cl N ₄ O ₃	529.037
9100	1020	1	000726403	9100-013	D 09	0.217	69.72	Spy4H	0.1776	TR0910001020	#NAME?	C ₃₀ H ₄₁ N ₃ O ₃	491.672
9100	2443	1	000727586	9100-035	C 07	0.383	69.62	Spy4H	0.1776	TR0910002443	#NAME?	C ₂₈ H ₃₅ Br N ₂ O ₃	527.5

Litray	Cmpd Lot	Expt Reg	Plate	Well	Raw Data	Assay Result	Conc(mM)	LionID	#NAME?	Chemical Structure	Molecular Formula	Mass
9100	850	1	000726233	9100-011 B 08	0.322	69.47	Spy4H	0.1776	TR0910000850		C ₃₀ H ₃₁ ClN ₂ O ₄	519.038
9100	851	1	000726234	9100-011 C 08	0.374	69.20	Spy4H	0.1776	TR0910000851		#NAME?	539.072
9100	3733	1	000728876	9100-051 E 08	0.332	68.93	Spy4H	0.1776	TR0910003733		#NAME?	593.695
9100											C ₃₆ H ₃₈ FN ₃ O ₄	593.695

Library	Cmpd	Lot	Exptg	Plate	Well	Raw Data	Assay Result	Assay	Conf	mg/ml	LionID	
9100	981	1	000726364	9100-013	E 04	0.321	68.63	Spy4H	0.1776	TR0910000981	#NAME?	C ₃₀ H ₃₈ Br N ₃ O ₄ 584.551
9100	2739	1	000727882	9100-039	C 04	0.205	68.58	Spy4H	0.1776	TR0910002739	H ₃ C ₂ N(H ₃ C) ₂ #NAME?	C ₃₁ H ₃₈ Cl N ₃ O ₄ 550.095
9100	2749	1	000727892	9100-039	E 05	0.252	68.29	Spy4H	0.1776	TR0910002749	H ₃ C ₂ N(H ₃ C) ₂ #NAME?	C ₃₂ H ₃₆ Cl N ₃ O ₄ 562.106

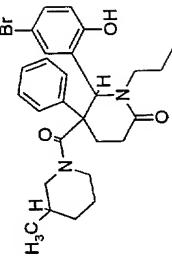
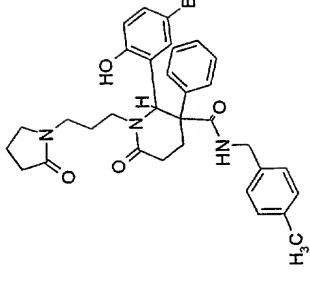
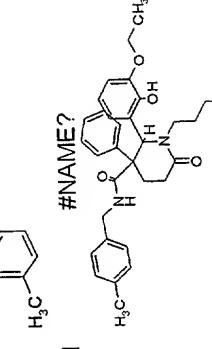
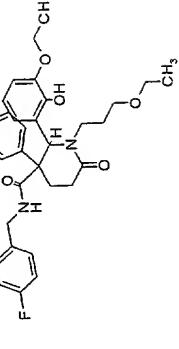
Library	Compd	ExReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	#NAME?	Chemical Structure	Molecular Formula	Molecular Weight
9100	2517	1	000727660	9100-036 E 06	0.402	68.27	Spy4H	0.1776	TR09100002517	#NAME?		C ₂₈ H ₂₈ Cl ₂ N ₂ O ₄	527.445
9100	854	1	000726237	9100-011 F 08	0.269	67.85	Spy4H	0.1776	TR0910000854	#NAME?		C ₃₁ H ₃₁ ClN ₄ O ₃	543.064
9100	1755	1	000726898	9100-023 C 11	0.363	67.80	Spy4H	0.1776	TR0910001755	#NAME?		C ₃₁ H ₃₄ N ₂ O ₃	482.621
9100													

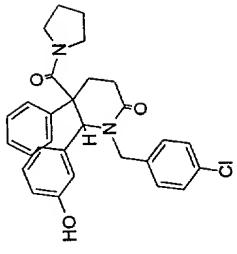
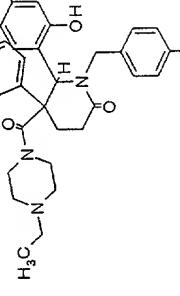
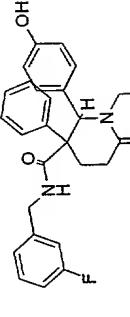
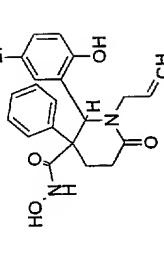
Library	Compound ID	Expt Reg.	Plate	Well	Raw Data	Assay Result	Assay	Conc	mg/ml	LionID		
9100	2429	1	000727572	9100-035	E 05	0.217	67.70	Spy4H	0.1776	TR0910002429	#NAME?	C ₃₃ H ₃₉ N ₃ O ₃
												525.689
9100	1092	1	000726475	9100-014	D 08	0.322	67.49	Spy4H	0.1776	TR0910001092	#NAME?	C ₂₈ H ₂₉ F N ₂ O ₃
												460.546
9100	613	1	000725996	9100-008	E 08	0.319	67.40	Spy4H	0.1776	TR0910000613	#NAME?	C ₂₈ H ₂₉ F N ₂ O ₃
												460.546
9100	845	1	000726228	9100-011	E 07	0.421	67.31	Spy4H	0.1776	TR0910000845	#NAME?	C ₃₀ H ₃₁ Cl N ₂ O ₃
												503.039

Library	Cmpd_1	Exptg	Plate	Well	Ran	Data	Assay	Result	Assay	Conc	Yield	LionID	#NAME?	C	H	N	O
9100	2324	1	000727467	9100-033	D 02	0.232	66.94	Spy4H	0.1776	TR0910002324				C ₃₁ H ₃₈ N ₄ O ₄			530.665
9100	2500	1	000727643	9100-036	D 04	0.368	66.93	Spy4H	0.1776	TR0910002500				C ₃₄ H ₃₉ Cl ₂ N ₃ O ₃			608.606
9100	700	1	000726083	9100-009	D 09	0.288	66.86	Spy4H	0.1776	TR0910000700				C ₃₄ H ₃₈ F ₃ N ₃ O ₃			593.686
9100	877	1	000726260	9100-011	E 11	0.255	66.77	Spy4H	0.1776	TR0910000877				C ₂₅ H ₂₃ Cl N ₂ O ₄			450.92

Library	Chpd_1	ExReg	Plate	Well	Raw Data	Assay Result	Assay	Cone. ng/ml	LionID	
9100	2595	1	000727738	9100-037	C 06	0.24	66.62	Spy4H	0.1776	TR0910002595
										#NAME?
										<chem>CN1CCCCC1[C@H]2[C@@H]1[C@H](C[C@H]1[C@H]2O)C(=O)CC[C@H]3[C@H]2[C@H]1[C@H]3Cc4ccc(O)cc4</chem>
9100	1013	1	000726396	9100-013	E 08	0.414	66.46	Spy4H	0.1776	TR0910001013
										#NAME?
										<chem>CN1CCCCC1[C@H]2[C@@H]1[C@H](C[C@H]1[C@H]2O)C(=O)CCCCCCCC[C@H]3[C@H]2[C@H]1[C@H]3Cc4ccc(O)cc4</chem>
9100	2731	1	000727874	9100-039	C 03	0.388	66.26	Spy4H	0.1776	TR0910002731
										#NAME?
										<chem>CN1CCCCC1[C@H]2[C@@H]1[C@H](C[C@H]1[C@H]2O)C(=O)CC[C@H]3[C@H]2[C@H]1[C@H]3Cc4ccc(O)cc4</chem>
9100	1710	1	000726853	9100-023	F 05	0.415	66.20	Spy4H	0.1776	TR0910001710
										#NAME?
										<chem>CC#CNC[C@H]1[C@H]2[C@H]1[C@H]3[C@H]2Cc4ccc(O)cc4[C@H]3CBr</chem>
										C ₂₅ H ₂₇ BrN ₂ O ₃
										483.403
										569.098
										565.754

Library	Compd	Lot	Expt Reg	Plate	Well	Raw Data	Assay	Result	Assay	Conc	mg/ml	LionID		
9100	662	1	000726045	9100-009	F 04	0.32	Spy4H	65.85	Spy4H	0.1776	TR0910000662	#NAME?	C ₃₁ H ₃₄ Cl ₂ N ₂ O ₄	569.526
9100	731	1	000726114	9100-010	C 03	0.283		65.76	Spy4H	0.1776	TR0910000731	#NAME?	C ₂₈ H ₃₀ N ₂ O ₃	442.556
9100	1702	1	000726845	9100-023	F 04	0.417		65.66	Spy4H	0.1776	TR0910001702	#NAME?	C ₂₇ H ₃₅ Br N ₂ O ₄	531.487
9100	2355	1	000727498	9100-033	C 06	0.452		65.53	Spy4H	0.1776	TR0910002355	#NAME?	C ₃₂ H ₄₂ N ₂ O ₄	518.694
9100	1955	1	000727098	9100-028	C 06	0.353		65.27	Spy4H	0.1776	TR0910001955	#NAME?	C ₃₁ H ₄₀ N ₂ O ₄	504.667

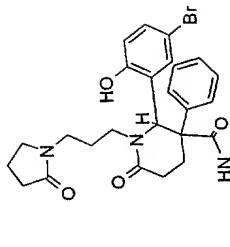
Library	Chord Lot	ExFrag	Plate	Well	Fay Data	Assay Result	Assay	Conc mg/ml	LionID	#NAME?	Chemical Structure	Molecular Formula	MW
9100	2475	1	000727618	9100-035	C 11	0.305	65.13	Spy4H	0.1776	TR0910002475		C ₃₀ H ₃₉ BrN ₂ O ₃	555.553
9100	971	1	000726354	9100-013	C 03	0.379	65.11	Spy4H	0.1776	TR0910000971		#NAME?	618.568
9100	2531	1	000727674	9100-036	C 08	0.302	65.06	Spy4H	0.1776	TR0910002531		#NAME?	544.688
9100	2533	1	000727676	9100-036	E 08	0.304	65.06	Spy4H	0.1776	TR0910002533		#NAME?	548.651

Library	Cmpd_16	ExReg	Plate	Well	Raw Data	Assay	Result	Assay	Conc mg/ml	LionID	
9100	843	1	000726226	9100-011	C 07	0.364	64.87	Spy4H	0.1776	TR0910000843	#NAME?
											
9100	2740	1	000727883	9100-039	D 04	0.384	64.80	Spy4H	0.1776	TR0910002740	#NAME?
											
9100	612	1	000725995	9100-008	D 08	0.339	64.80	Spy4H	0.1776	TR0910000612	#NAME?
											
9100	237	1	000725620	9100-003	E 11	0.281	64.74	Spy4H	0.1776	TR0910000237	#NAME?
											
9100											

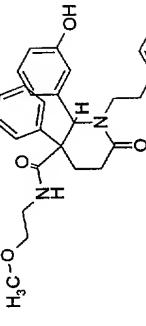
Library	Cmpd	Lot	Expt Reg	Plate	Well	Raw Data	Assay Result	Category	LionID	
9100	2330	1	000727473	9100-033	B 03	0.281	64.69	Spy4H	0.1776	TR0910002330
9100	4100	1	000729243	9100-057	D 04	0.261	64.67	Spy4H	0.1776	TR0910004100
9100	595	1	000725978	9100-008	C 06	0.339	64.51	Spy4H	0.1776	TR0910000595
9100	2470	1	000727613	9100-035	F 10	0.294	64.49	Spy4H	0.1776	TR0910002470
								#NAME?		C ₃₁ H ₄₀ N ₂ O ₅
								C ₃₂ H ₃₄ F ₃ N ₃ O ₃		520.666
								#NAME?		C ₃₂ H ₃₄ F ₃ N ₃ O ₃
								C ₂₈ H ₃₆ N ₂ O ₃		565.633
								#NAME?		C ₂₈ H ₃₆ N ₂ O ₃
								#NAME?		C ₂₇ H ₃₁ Br N ₂ O ₃
								H ₃ C		511.457

9100 973 1 000726356 9100-013 E 03 0.304 64.02 Spy4H 0.1776 TR0910000973

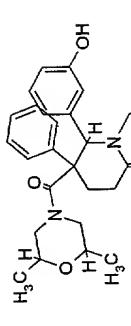
Library Cmpd Lot ExReg Plate Well Raw Data Assay Result Assay Core mg/ml LionID
9100 973 1 000726356 9100-013 E 03 0.304 64.02 Spy4H 0.1776 TR0910000973



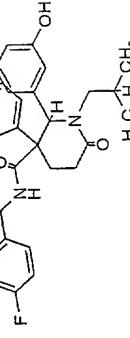
9100 647 1 000726030 9100-009 G 02 0.295 63.83 Spy4H 0.1776 TR0910000647



9100 878 1 000726261 9100-011 F 11 0.356 63.79 Spy4H 0.1776 TR0910000878



9100 573 1 000725956 9100-008 E 03 0.359 63.64 Spy4H 0.1776 TR0910000573



C₃₂ H₃₃ Br F N₃ O₄ #NAME?

622.532

C₂₉ H₃₀ Cl₂ N₂ O₄ #NAME?

541.473

C₃₁ H₃₃ Cl N₂ O₄ #NAME?

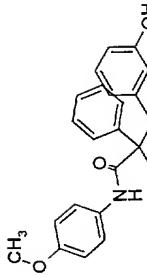
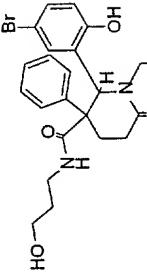
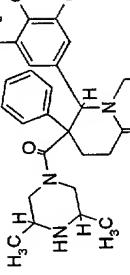
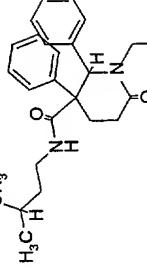
533.065

C₂₈ H₃₁ F N₂ O₃ #NAME?

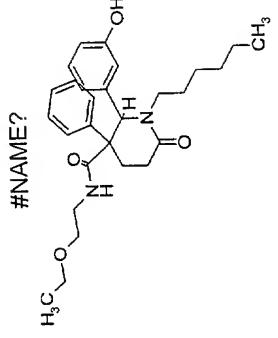
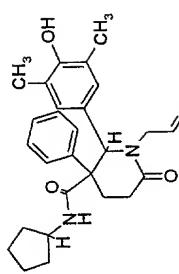
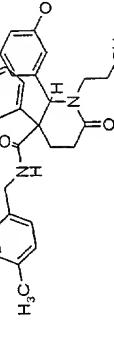
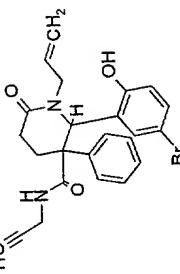
474.573

Library	Cmpd	Expt Reg.	Plate	Well	Raw Data	Assay Result	Conc mg/ml	LionID	
9100	2235	1	000727378	9100-031 C 11	0.239	63.59	Spy4H	0.1776	TR0910002235
9100	2422	1	000727565	9100-035 F 04	0.259	63.53	Spy4H	0.1776	TR0910002422
9100	847	1	000726230	9100-011 G 07	0.292	63.52	Spy4H	0.1776	TR0910000847
9100	1014	1	000726397	9100-013 F 08	0.247	63.48	Spy4H	0.1776	TR0910001014
							#NAME?		C ₃₆ H ₄₃ N ₃ O ₃
							#NAME?		C ₃₂ H ₃₈ N ₂ O ₄
							#NAME?		C ₂₈ H ₂₉ ClN ₂ O ₄
							#NAME?		C ₃₀ H ₃₈ N ₄ O ₃

Library	Cmpd	Lot	ExPReg	Plate	Well	Raw Data	Assay Result	Conc	NAME?	LionID	Chem3D	MW	
9100	3751	1	000728894	9100-051	G 10	0.289	63.44	Spy4H	0.1776	TR09100003751	#NAME?	C ₃₅ H ₃₇ N ₃ O ₄ S	595.76
9100	589	1	000725972	9100-008	E 05	0.225	63.35	Spy4H	0.1776	TR0910000589	#NAME?	C ₂₈ H ₃₇ N ₃ O ₃	463.618
9100	4155	1	000729298	9100-057	C 11	0.321	63.27	Spy4H	0.1776	TR0910004155	#NAME?	C ₃₈ H ₄₇ N ₃ O ₃	593.807
9100	1683	1	000726826	9100-023	C 02	0.484	63.25	Spy4H	0.1776	TR0910001683	#NAME?	C ₂₆ H ₃₁ BrN ₂ O ₃	499.446

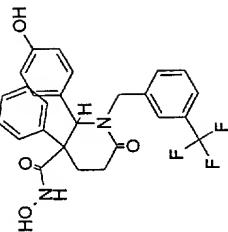
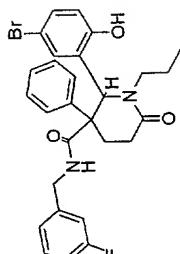
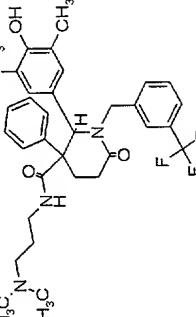
Library	Cmpd ID	Expt Reg.	Plate	Well	Raw Data	Assay	Result	Conc / molar	LionID		
9100	596	1	000725979	9100-008	D 06	0.286	63.06	Spy4H	0.1776	TR0910000596	#NAME?
											
9100	1707	1	000726850	9100-023	C 05	0.352	62.99	Spy4H	0.1776	TR0910001707	#NAME?
											
9100	2629	1	000727772	9100-037	E 10	0.275	62.89	Spy4H	0.1776	TR0910002629	#NAME?
											
9100	581	1	000725964	9100-008	E 04	0.326	62.77	Spy4H	0.1776	TR0910000581	#NAME?
											
9100											

Libran	Cmpd Lo	Expt Reg	Plate	Well	Raw Data	Assay Result	Assay Concentration	LionID	LionID	
9100	1038	1	000726421	9100-013 F 11	0.295	62.40	Spy4H	0.1776	TR0910001038	#NAME?
										C ₃₀ H ₄₀ N ₂ O ₄
										492.656
9100	773	1	000726156	9100-010 E 08	0.231	62.39	Spy4H	0.1776	TR0910000773	#NAME?
										C ₃₀ H ₃₁ F N ₂ O ₃
										486.584
9100	1971	1	000727114	9100-028 C 08	0.296	61.99	Spy4H	0.1776	TR0910001971	#NAME?
										C ₃₁ H ₃₆ N ₂ O ₄
										500.635
9100	2478	1	000727621	9100-035 F 11	0.265	61.92	Spy4H	0.1776	TR0910002478	#NAME?
										C ₃₀ H ₃₉ Br N ₂ O ₄
										571.552

Library	Compound ID	Expt Reg.	Plate	Well	Raw Data	Assay Result	Assay	Conc	LionID	#NAME?	Chemical Structure	Formula	MW	
9100	1028	1	000726411	9100-013	D 10	0.257	61.86	Spy4H	0.1776	TR0910001028	#NAME?		C ₂₈ H ₃₈ N ₂ O ₄	466.618
9100	1045	1	000726428	9100-014	E 02	0.331	61.83	Spy4H	0.1776	TR0910001045	#NAME?		C ₂₈ H ₃₄ N ₂ O ₃	446.588
9100	1091	1	000726474	9100-014	C 08	0.346	61.83	Spy4H	0.1776	TR0910001091	#NAME?		C ₂₉ H ₃₂ N ₂ O ₃	456.583
9100	230	1	000725613	9100-003	F 10	0.323	61.69	Spy4H	0.1776	TR0910000230	#NAME?		C ₂₄ H ₂₃ BrN ₂ O ₃	467.361

Library	Compound ID	Expt ID	Plate	Well	Raw Data	Assay Result	Assay	Contaminant	LionID	#NAME?	
9100	855	1	000726238	9100-011	G 08	0.344	61.63	Spy4H	0.1776	TR0910000855	C ₂₈ H ₂₇ ClN ₂ O ₃
											474.985
9100	3741	1	000728884	9100-051	E 09	0.246	61.60	Spy4H	0.1776	TR0910003741	#NAME?
											555.715
9100	2213	1	000727356	9100-031	E 08	0.271	61.41	Spy4H	0.1776	TR0910002213	H ₃ C(CH ₃) ₂
											591.723

Library	Compound ID	Expt Reg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	#NAME?	C ₃₁ H ₂₉ ClN ₂ O ₄ S	561.099
9100	2738	1	000727881	9100-039	B 04	0.398	61.32	Spy4H	0.1776	TR0910002738	#NAME?	
9100	979	1	000726362	9100-013	C 04	0.245	61.31	Spy4H	0.1776	TR0910000979	#NAME?	
9100	1019	1	000726402	9100-013	C 09	0.239	61.31	Spy4H	0.1776	TR0910001019	H ₃ C-N CH ₃	C ₂₉ H ₄₁ N ₃ O ₃
9100												479.661

Library	Cmpd	Lot	Exptg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	#NAME?	Chemical Structure	Molecular Formula	Exact Mass
9100	4117	1	000729260	9100-057	E 06	0.279	61.30	Spy4H	0.1776	TR0910004117	#NAME?		C ₂₆ H ₂₃ F ₃ N ₂ O ₄	484.472
9100	2452	1	000727595	9100-035	D 08	0.327	61.28	Spy4H	0.1776	TR0910002452	#NAME?		C ₃₁ H ₃₄ BrF ₃ N ₂ O ₃	581.523
9100	699	1	000726082	9100-009	C 09	0.215	61.13	Spy4H	0.1776	TR0910000699	#NAME?		C ₃₃ H ₃₃ F ₃ N ₃ O ₃	581.675

Library	Compound ID	Expt Reg	Plate	Well	Raw Data	Assay Result	Assay	Conc (ug/ml)	LionID		
9100	1756	1	000726899	9100-023	D 11	0.289	61.11	Spy4H	0.1776	TR0910001756	#NAME?
											C ₃₂ H ₃₀ N ₂ O ₄
											506.599
9100	1002	1	000726385	9100-013	B 07	0.24	61.04	Spy4H	0.1776	TR0910001002	#NAME?
											C ₃₀ H ₄₁ N ₃ O ₃
											491.672
9100	1004	1	000726387	9100-013	D 07	0.242	61.04	Spy4H	0.1776	TR0910001004	#NAME?
											C ₂₉ H ₃₆ N ₄ O ₃
											488.628

Library	Chipped Lot	Expt Reg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	
9100	621	1	000726004	9100-008	E 09	0.29	61.03	Spy4H	0.1776	TR0910000621
9100	2221	1	000727364	9100-031	E 09	0.251	60.87	Spy4H	0.1776	TR0910002221
9100	689	1	000726072	9100-009	A 08	0.249	60.79	Spy4H	0.1776	TR0910000689
9100	2322	1	000727465	9100-033	B 02	0.255	60.75	Spy4H	0.1776	TR0910002322
9100	2969	1	000728112	9100-042	A 03	0.328	60.74	Spy4H	0.1776	TR0910002969
										C ₂₆ H ₃₄ N ₂ O ₃
										422.566
										C ₃₅ H ₄₃ N ₃ O ₃
										553.743
										C ₃₃ H ₃₆ F ₃ N ₃ O ₃
										579.659
										C ₃₂ H ₄₃ N ₃ O ₄
										533.709
										C ₃₁ H ₃₃ Cl ₂ N ₃ O ₃
										566.526

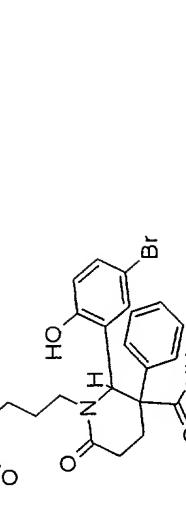
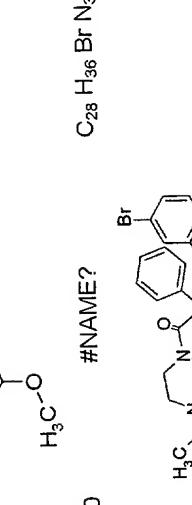
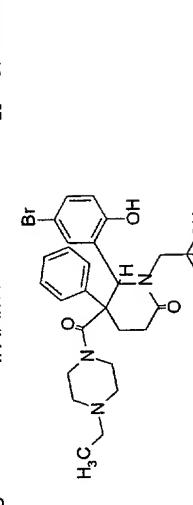
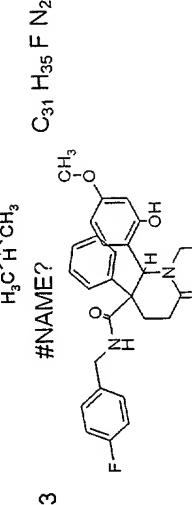
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9100	849	1	000726232	9100-011 A 08	0.295		60.55	Spy4H	0.1776	TR0910000849				
9100	866	1	000726249	9100-011 B 10	0.398		60.55	Spy4H	0.1776	TR0910000866				
9100	873	1	000726256	9100-011 A 11	0.371		60.55	Spy4H	0.1776	TR0910000873				
9100	605	1	000725988	9100-008 E 07	0.254		60.46	Spy4H	0.1776	TR0910000605				

Library	Cmpd Loc	Ext Reg	Plate	Well	Ray Data	Assay Result	Assay	Conc mg/ml	LionID	#NAME?	
9100	3752	1	000728895	9100-051 H 10	0.258	60.38	Spy4H	0.1776	TR0910003752	C ₃₃ H ₃₉ N ₃ O ₄	541.688
9100	2461	1	000727604	9100-035 E 09	0.402	60.32	Spy4H	0.1776	TR0910002461		#NAME?
9100	990	1	000726373	9100-013 F 05	0.26	60.23	Spy4H	0.1776	TR0910000990		#NAME?
9100											

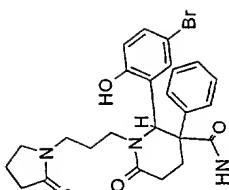
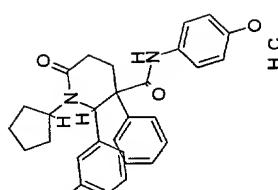
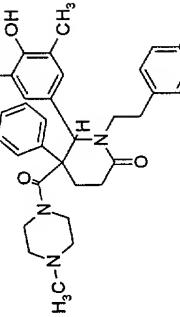
Librar	Cmpd	Loc	ExptReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	#NAME?	
9100	711	1	000726094	9100-009	G 10	0.388	60.12	Spy4H	0.1776	TR0910000711	C ₃₄ H ₃₃ F ₃ N ₂ O ₃ S	606.706
9100	2436	1	000727579	9100-035	D 06	0.314	60.00	Spy4H	0.1776	TR0910002436	#NAME?	
9100	2339	1	000727482	9100-033	C 04	0.257	59.91	Spy4H	0.1776	TR0910002339	#NAME?	
9100	572	1	000725955	9100-008	D 03	0.338	59.88	Spy4H	0.1776	TR0910000572	#NAME?	

Library	Cmpd	Loc	ExReg	Plate	Well	Raw Data	Assay	Result	Assay	Conc	Unit	LionID			
9100	1061	1	000726444	9100-014	E 04	0.403	59.84	Spy4H	0.1776	TR0910001061	#NAME?		C ₂₈ H ₃₆ N ₂ O ₃		448.603
9100	857	1	000726240	9100-011	A 09	0.265	59.74	Spy4H	0.1776	TR0910000857	#NAME?		C ₂₇ H ₂₇ ClN ₂ O ₄		478.973
9100	861	1	000726244	9100-011	E 09	0.427	59.74	Spy4H	0.1776	TR0910000861	#NAME?		C ₃₀ H ₃₃ ClN ₂ O ₃		505.055
9100	2637	1	000727780	9100-037	E 11	0.35	59.73	Spy4H	0.1776	TR0910002637	#NAME?		C ₂₇ H ₂₇ ClN ₂ O ₄		478.973

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Library	Compound ID	Expt Reg.	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID
9100	996	1	000726379	9100-013	D 06	0.279	59.69	Spy4H	0.1776	TR0910000996			C ₃₂ H ₃₄ BrN ₃ O ₅	620.541					
9100	1700	1	000726843	9100-023	D 04	0.316	59.50	Spy4H	0.1776	TR0910001700		#NAME?	B ₂₈ H ₃₆ BrN ₃ O ₃	542.514					
9100	813	1	000726196	9100-011	E 03	0.38	59.47	Spy4H	0.1776	TR0910000813		#NAME?	C ₃₁ H ₃₅ FN ₂ O ₅	534.625					

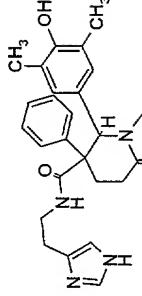
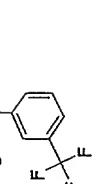
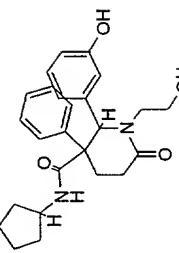
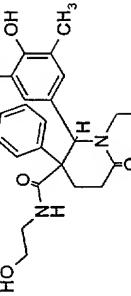
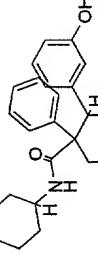
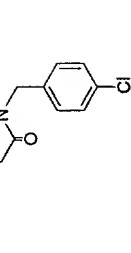
9100 2489 1 000727632 9100-036 A 03 0.361 59.45 Spy4H 0.1776 TR0910002489

Library	Cmpd	Lo	ExReg	Plate	Well	Raw Data	Assay	Result	LionID	Conc(mM)	#NAME?	Chemical Structure	Molecular Formula	Mass
9100	988	1	000726371	9100-013	D 05	0.247	59.42	Spy4H	0.1776	TR0910000988	#NAME?		C ₂₉ H ₃₆ BrN ₃ O ₅	586.523
9100	3236	1	000728379	9100-045	D 06	0.304	59.42	Spy4H	0.1776	TR0910003236	#NAME?		C ₃₀ H ₃₂ N ₂ O ₄	484.593
9100	2489	1	000727632	9100-036	A 03	0.361	59.45	Spy4H	0.1776	TR0910002489	#NAME?		C ₃₃ H ₃₇ Cl ₂ N ₃ O ₃	594.579

Library	Cmpd_Lot	ExReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID		
9100	2438	1	000727581	9100-035 F 06	0.285	59.36	Spy4H	0.1776	TR0910002438	#NAME?	C ₃₃ H ₃₈ N ₂ O ₄
9100	1115	1	000726498	9100-014 C 11	0.262	59.28	Spy4H	0.1776	TR0910001115	#NAME?	C ₂₇ H ₃₄ N ₂ O ₃
9100	1701	1	000726844	9100-023 E 04	0.512	59.24	Spy4H	0.1776	TR0910001701	#NAME?	C ₂₇ H ₃₅ BrN ₂ O ₃
9100	1718	1	000726861	9100-023 F 06	0.364	59.24	Spy4H	0.1776	TR0910001718	#NAME?	C ₂₈ H ₃₅ BrN ₂ O ₄
											543.498

Library	Cmpd Lot	Ex Reg	Plate	Well	Raw Data	Assay Result	Conc mg/ml	LionID	
9100	1733	1	000726876	9100-023	E 08	0.331	59.24	Spy4H	0.1776
								TR09100001733	#NAME?
									C ₃₂ H ₂₉ F N ₂ O ₃
									508.59
9100	835	1	000726218	9100-011	C 06	0.321	59.20	Spy4H	0.1776
								TR0910000835	#NAME?
									C ₃₀ H ₄₀ N ₂ O ₅
									508.655
9100	1022	1	000726405	9100-013	F 09	0.261	59.15	Spy4H	0.1776
								TR0910001022	#NAME?
									C ₂₉ H ₄₀ N ₂ O ₄
									480.645

Library	Compound ID	ExReg	Plate	Well	Raw Data	Assay	Result	Assay	Conc/mg/ml	LionID	
9100	2454	1	000727597	9100-035 F 08	0.283	59.04	Spy4H	0.1776	TR0910002454	#NAME?	C ₃₀ H ₃₇ BrN ₄ O ₃
9100	1723	1	000726866	9100-023 C 07	0.289	58.97	Spy4H	0.1776	TR0910001723	H ₃ C	#NAME?
9100	1714	1	000726857	9100-023 B 06	0.335	58.70	Spy4H	0.1776	TR0910001714	#NAME?	C ₂₉ H ₃₀ N ₂ O ₃
9100											454.567
9100											498.418

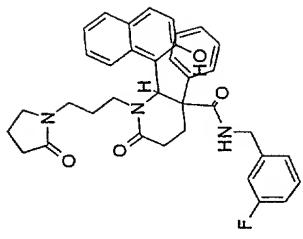
Library	Cmpd Lot	EPR Reg	Plate	Well	Raw Data	Assay Result	Assay Comment	LionID	
9100	684	1	000726067	9100-009	D 07	0.231	58.43	Spy4H	0.1776 TR0910000684
									#NAME?
									C ₃₃ H ₃₃ F ₃ N ₄ O ₃
9100	1085	1	000726468	9100-014	E 07	0.26	58.43	Spy4H	0.1776 TR0910001085
									#NAME?
									C ₂₆ H ₃₂ N ₂ O ₃
9100	2417	1	000727560	9100-035	A 04	0.302	58.40	Spy4H	0.1776 TR0910002417
									#NAME?
									C ₂₉ H ₃₂ N ₂ O ₄
9100	848	1	000726231	9100-011	H 07	0.279	58.38	Spy4H	0.1776 TR0910000848
									#NAME?
									C ₃₁ H ₃₃ ClN ₂ O ₃
									511.066
									590.643

Library	Cmpd	Lot	Ex Reg	Plate	Well	Raw Data	Assay	Result	Assay	Conc mg/ml	LionID		
9100	2484	1	000727627	9100-036	D 02	0.319	58.38	Spy4H	0.1776	TR0910002484	#NAME?	C ₃₃ H ₃₄ Cl ₂ N ₄ O ₃	605.563
9100	202	1	000725585	9100-003	B 07	0.243	58.34	Spy4H	0.1776	TR0910000202	#NAME?	C ₂₇ H ₃₂ Br N ₃ O ₃	526.472
9100	210	1	000725593	9100-003	B 08	0.331	58.34	Spy4H	0.1776	TR0910000210	#NAME?	C ₂₆ H ₂₉ Br N ₂ O ₄	513.429
9100	3029	1	000728172	9100-042	E 10	0.279	58.29	Spy4H	0.1776	TR0910003029	#NAME?	C ₃₁ H ₄₃ N ₃ O ₄	521.698

Liber	Cmpd	Lot	ExReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	
9100	1972	1	000727115	9100-028	D 08	0.284	58.15	Spy4H	0.1176	TR09100001972	#NAME?
9100	635	1	000726018	9100-008	C 11	0.326	58.14	Spy4H	0.1776	TR0910000635	#NAME?
9100	2212	1	000727355	9100-031	D 08	0.281	58.14	Spy4H	0.1776	TR0910002212	#NAME?
9100	2458	1	000727601	9100-035	B 09	0.285	58.08	Spy4H	0.1776	TR0910002458	#NAME?
											C ₃₀ H ₃₃ F N ₂ O ₄
											504.599
											C ₂₇ H ₃₄ N ₂ O ₃
											434.577
											C ₃₇ H ₃₈ F N ₃ O ₃
											591.723
											C ₂₉ H ₃₃ Br N ₂ O ₃ S
											569.561

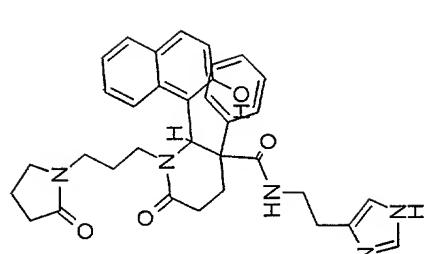
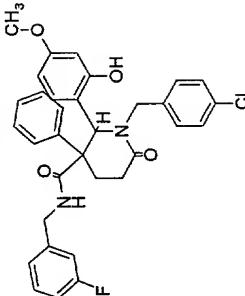
Library	Cmpd	Lot	ExReg	Plate	Well	Raw Data	Assay	Conc/mg/ml	LionID		
9100	980	1	000726363	9100-013	D 04	0.254	58.06	Spy4H	0.1776	TR0910000980	#NAME?
											C ₃₁ H ₃₈ Br N ₄ O ₄
											611.577
9100	2446	1	000727589	9100-035	F 07	0.408	57.76	Spy4H	0.1776	TR0910002446	#NAME?
											C ₂₇ H ₃₃ Br N ₂ O ₃ S
											513.473
9100	2465	1	000727608	9100-035	A 10	0.25	57.76	Spy4H	0.1776	TR0910002465	#NAME?
											C ₂₈ H ₃₇ Br N ₂ O ₃ S
											561.581

Library	Cmpd	Lot	EntReg	Plate	Wells	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	
9100	3732	1	000728875	9100-051 D 08	0.312	57.63	Spy4H	0.1776	TR09100003732	#NAME?	C ₃₈ H ₃₈ F N ₃ O ₄
											593.695



Library	Cmpd	Lot	EntReg	Plate	Wells	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	
9100	2435	1	000727578	9100-035 C 06	0.395	57.43	Spy4H	0.1776	TR0910002435	#NAME?	C ₃₃ H ₃₈ N ₂ O ₃
											510.674
9100	811	1	000726194	9100-011 C 03	0.377	57.30	Spy4H	0.1776	TR0910000811	#NAME?	C ₃₂ H ₃₈ N ₂ O ₅
											530.661

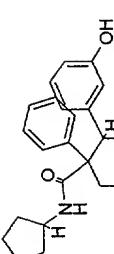
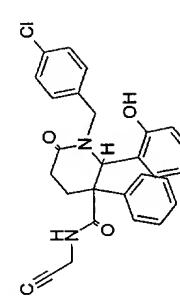
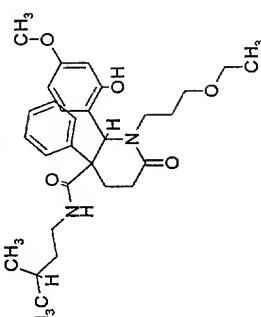
Library	Cmpd	Lot	ExReg	Plate	Well	Raw Data	Assay Result	Assay	Conc/mg/ml	LionID	#NAME?		C ₂₉ H ₂₇ Cl ₂ N ₃ O ₃	536.456	
9100	2994	1	000728137	9100-042	B 06	0.413	57.20	Spy4H	0.1776	TR0910002994					
9100	2620	1	000727763	9100-037	D 09	0.268	57.14	Spy4H	0.1776	TR0910002620	#NAME?				560.134
9100	2580	1	000727723	9100-037	D 04	0.243	56.86	Spy4H	0.1776	TR0910002580	#NAME?				580.769
9100	4082	1	000729225	9100-057	B 02	0.248	56.80	Spy4H	0.1776	TR0910004082	#NAME?				565.633

Liber	Cmpd	Lot	Expteg	Plate	Well	Raw Data	Assay Result	Conc mg/ml	LionID	#NAME?	C ₃₂ H ₂₉ ClN ₂ O ₄	541.044
9100	876	1	000726259	9100-011	D 11	0.432	56.76	Spy4H	0.1776	TR0910000876		
9100	3724	1	000728867	9100-051	D 07	0.252	56.72	Spy4H	0.1776	TR0910003724		C ₃₄ H ₃₇ N ₅ O ₄ 579.697
9100	2732	1	000727875	9100-039	D 03	0.457	56.68	Spy4H	0.1776	TR0910002732		C ₃₃ H ₃₀ ClFN ₂ O ₄ 573.061

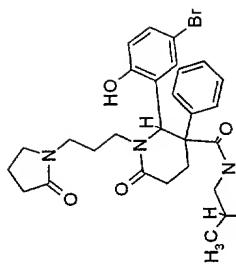
Chemical structures and associated assay results for compounds 9100-196, 9100-836, 9100-871, and 9100-1.

Liber	Cmpd	Lot	E Reg	Plate	Well	Raw Data	Assay Result	Conc mg/ml	LionID	#NAME?	Chemical Structure	Molecular Formula	PubChem ID
9100	196	1	000725579	9100-003	D 06	0.252	56.51	Spy4H	0.1776	TR0910000196		C ₂₆ H ₂₆ N ₂ O ₄	430.501
9100	836	1	000726219	9100-011	D 06	0.304	56.49	Spy4H	0.1776	TR0910000836		C ₃₁ H ₃₆ N ₂ O ₆	532.633
9100	871	1	000726254	9100-011	G 10	0.336	56.49	Spy4H	0.1776	TR0910000871		#NAME?	
9100	871	1	000726254	9100-011	G 10	0.336	56.49	Spy4H	0.1776	TR0910000871		C ₃₁ H ₂₉ ClN ₂ O ₃ S	545.1

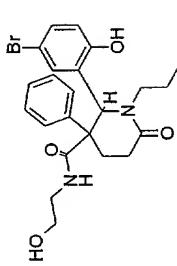
Lipan	Cmpd	Loc	E/Freq	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID		
9100	2453	1	000727596	9100-035	E 08	0.43	56.47	Spy4H	0.1776	TR09100002453	#NAME?	C ₃₁ H ₃₄ Br F N ₂ O ₃
9100	1053	1	000726436	9100-014	E 03	0.478	56.44	Spy4H	0.1776	TR0910001053	#NAME?	C ₃₀ H ₃₁ F N ₂ O ₃
9100	1116	1	000726499	9100-014	D 11	0.265	56.44	Spy4H	0.1776	TR0910001116	#NAME?	C ₂₈ H ₃₀ N ₂ O ₄
9100	997	1	000726380	9100-013	E 06	0.254	56.44	Spy4H	0.1776	TR0910000997	#NAME?	C ₂₅ H ₂₈ Br N ₃ O ₅
												530.416
												581.523

Libian	Cmpd	Lot	ExReg	Plate	Well	Raw Data	Assay Result	Assay	Conc/mg/ml	LionID	
9100	565	1	000725948	9100-008	E 02	0.304	56.40	Spy4H	0.1776	TR0910000565	#NAME?
											
9100	2750	1	000727893	9100-039	F 05	0.457	56.39	Spy4H	0.1776	TR0910002750	#NAME?
											
9100	821	1	000726204	9100-011	E 04	0.322	56.22	Spy4H	0.1776	TR0910000821	#NAME?
											
9100											

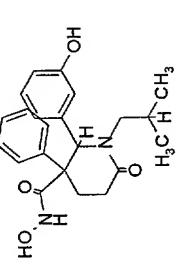
Liber	Comp	Lot	ExReg	Plate	Well	Raw Data	Assay	Result	Assay	Conc mg/ml	LionID	
9100	989	1	000726372	9100-013	E 05	0.257	56.17	Spy4H	0.1776	TR0910000989	#NAME?	C ₃₁ H ₃₉ Br N ₄ O ₄



Liber	Comp	Lot	ExReg	Plate	Well	Raw Data	Assay	Result	Assay	Conc mg/ml	LionID	
9100	2457	1	000727600	9100-035	A 09	0.275	56.15	Spy4H	0.1776	TR0910002457	#NAME?	C ₂₆ H ₃₃ Br N ₂ O ₄



Liber	Comp	Lot	ExReg	Plate	Well	Raw Data	Assay	Result	Assay	Conc mg/ml	LionID	
9100	597	1	000725980	9100-008	E 06	0.25	56.11	Spy4H	0.1776	TR0910000597	#NAME?	C ₂₂ H ₂₆ N ₂ O ₄



Liber	Cmpd	Loc	ExReg	Plate	W#	RawData	Assay	Result	Assay	Concng(m)	LionID	#NAME?	C ₃₃ H ₃₉ N ₃ O ₄	541.688
9100	3746	1	00072889	9100-051	B 10	0.268	56.11	Spy4H	0.1776	TR09100003746	#NAME?			
9100	660	1	000726043	9100-009	D 04	0.433	56.07	Spy4H	0.1776	TR0910000660	#NAME?	C ₃₂ H ₃₅ Cl ₂ N ₃ O ₃	580.552	
9100	2541	1	000727684	9100-036	E 09	0.289	55.98	Spy4H	0.1776	TR0910002541	#NAME?	C ₃₀ H ₄₂ N ₂ O ₅	510.671	
9100	3203	1	000728346	9100-045	C 02	0.392	55.92	Spy4H	0.1776	TR0910003203	#NAME?	C ₂₇ H ₃₂ N ₂ O ₃	432.561	

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#NAME? C₂₈H₃₄BrN₃O₅ 572.497

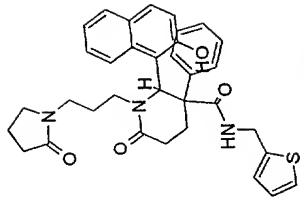
9100	2403	1	000727546	9100-035 C 02	0.434	55.83	Spy4H	0.1776	TR0910002403	.1.	#NAME?	C ₃₁ H ₃₄ N ₂ O ₃	482.621
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9100	3721	1	000728864	9100-051	^07	0.298	55.80	Spy4H	0.1776	TR0910003721	#NAME?	C ₃₅ H ₄₀ N ₄ O ₅	596.724
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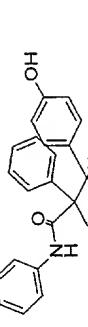
$$\text{C}_{35}\text{H}_{40}\text{N}_4\text{O}_5$$

$\text{C}_{28} \text{H}_{34} \text{BrN}_3\text{O}_6$ <chem>CC(=O)N1CC[C@H]2[C@H]1Cc3cc(O)c(cc3Br)C(C(=O)NCCCCCO)C2</chem> #NAME?	$\text{C}_{31} \text{H}_{34} \text{N}_2\text{O}_3$ <chem>CC(=O)N1CC[C@H]2[C@H]1Cc3cc(O)c(cc3Br)C(C(=O)NCCCCCO)C2C1CCN(C1)CC1</chem> #NAME?	$\text{C}_{35} \text{H}_{40} \text{N}_4\text{O}_5$ <chem>CC(=O)N1CC[C@H]2[C@H]1Cc3cc(O)c(cc3Br)C(C(=O)NCCCCCO)C2C1CCN(C1)CC[C@H]3[C@H]1[C@H]3Cc4ccccc4N3C1</chem> #NAME?
572.497 <chem>CC(=O)N1CC[C@H]2[C@H]1Cc3cc(O)c(cc3Br)C(C(=O)NCCCCCO)C2</chem>	482.621 <chem>CC(=O)N1CC[C@H]2[C@H]1Cc3cc(O)c(cc3Br)C(C(=O)NCCCCCO)C2C1CCN(C1)CC1</chem>	596.724 <chem>CC(=O)N1CC[C@H]2[C@H]1Cc3cc(O)c(cc3Br)C(C(=O)NCCCCCO)C2C1CCN(C1)CC[C@H]3[C@H]1[C@H]3Cc4ccccc4N3C1</chem>

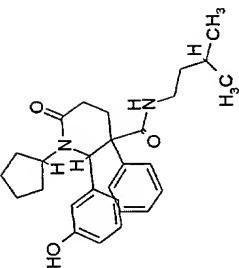
LibID	Cmpd Lot	Expt Reg	Plate	Well	Raw Data	Assay Result	Assay Concentration	LionID	#NAME?	C ₃₄ H ₃₅ N ₃ O ₄ S	581.734
9100	3738	1	000728881	9100-051 B 09	0.275	55.80	Spy4H	0.1776	TR0910003738		



LibID	Cmpd Lot	Expt Reg	Plate	Well	Raw Data	Assay Result	Assay Concentration	LionID	#NAME?	C ₃₇ H ₃₉ N ₃ O ₄	589.732
9100	2596	1	000727739	9100-037 D 06	0.263	55.71	Spy4H	0.1776	TR0910002596		



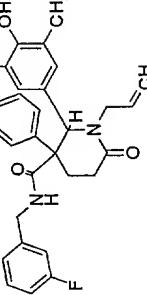
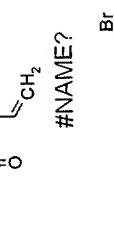
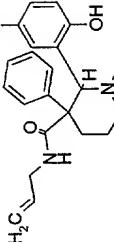
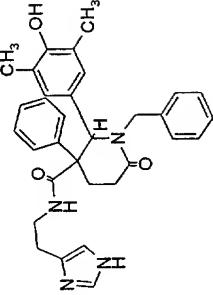
LibID	Cmpd Lot	Expt Reg	Plate	Well	Raw Data	Assay Result	Assay Concentration	LionID	#NAME?	C ₂₈ H ₃₆ N ₂ O ₃	448.603
9100	3221	1	000728364	9100-045 E 04	0.375	55.66	Spy4H	0.1776	TR0910003221		



LionID	Cmpd	Lot	E_HReg	Plate	Wst	Raw Data	Assay	Conc ng/ml	LionID		
9100	3235	1	000728378	9100-045	C 06	0.352	55.66	Spy4H	0.1776	TR0910003235	#NAME?
											C ₂₈ H ₃₆ N ₂ O ₃
											460.614
9100	3722	1	000728865	9100-051	B 07	0.26	55.50	Spy4H	0.1776	TR0910003722	#NAME?
											C ₃₆ H ₄₂ N ₄ O ₄
											582.741
9100	702	1	000726085	9100-009	F 09	0.29	55.40	Spy4H	0.1776	TR0910000702	#NAME?
											C ₃₃ H ₃₇ F ₃ N ₂ O ₄
											582.659
9100	1051	1	000726434	9100-014	C 03	0.422	55.31	Spy4H	0.1776	TR0910001051	#NAME?
											C ₃₁ H ₃₄ N ₂ O ₃
											482.621

Library Comp ID	Lot	Ex Reg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	#NAME?	Conc mg/ml	LionID	#NAME?	Conc mg/ml	LionID	#NAME?	Conc mg/ml	LionID	#NAME?	Conc mg/ml	LionID
9100	1070	1	000726453	9100-014	F 05	0.255	55.31	Spy4H	TR0910001070		C ₂₆ H ₂₈ N ₂ O ₃	416.518		C ₂₉ H ₃₆ N ₂ O ₄	476.619						
9100	1078	1	000726461	9100-014	F 06	0.255	55.31	Spy4H	0.1776		#NAME?	476.619		C ₂₉ H ₃₆ N ₂ O ₄	476.619						
9100	3725	1	000728868	9100-051	E 07	0.264	55.19	Spy4H	0.1776		#NAME?	553.699		C ₃₄ H ₃₉ N ₃ O ₄	553.699						

Liber	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay	Result	Assay	Conc ng/ml	LionID	
9100	1973	1	000727116	9100-028	E 08	0.28	55.14	Spy4H	0.1776	TR0910001973	#NAME?	C ₃₀ H ₃₃ F N ₂ O ₄
9100	1005	1	000726388	9100-013	E 07	0.445	55.08	Spy4H	0.1776	TR0910001005	#NAME?	C ₂₉ H ₃₈ N ₂ O ₃
9100	1066	1	000726449	9100-014	B 05	0.305	55.03	Spy4H	0.1776	TR0910001066	#NAME?	C ₂₇ H ₃₄ N ₂ O ₃
9100	863	1	000726246	9100-011	G 09	0.487	54.87	Spy4H	0.1776	TR0910000863	#NAME?	C ₃₃ H ₃₇ Cl N ₂ O ₃

LionID	Cmpd Lot	ExReg	Plate	Well	Raw Data	Assay Result	Assay	Conc ng/ml	LionID	
9100	1052	1	000726435	9100-014 D 03	0.419	54.75	Spy4H	0.1776	TR0910001052	#NAME?
										
9100	1077	1	000726460	9100-014 E 06	0.257	54.75	Spy4H	0.1776	TR0910001077	#NAME?
										
9100	206	1	000725589	9100-003 F 07	0.305	54.68	Spy4H	0.1776	TR0910000206	#NAME?
										
9100	2404	1	000727547	9100-035 D 02	0.242	54.55	Spy4H	0.1776	TR0910002404	#NAME?
										
										C ₃₀ H ₃₁ F N ₂ O ₃
										486.584
										C ₂₃ H ₂₆ N ₂ O ₄
										394.468
										C ₂₄ H ₂₅ BrN ₂ O ₃
										469.376
										C ₃₂ H ₃₄ N ₄ O ₃
										522.646

Librar	Cmpd Lo	ExReg	Plate	Well	Raw Data	Assay	Result	Assay	Conc ng/ml	LionID	
9100	687	1	000726070	9100-009 G 07	0.351	54.38	Spy4H	0.1776	TR0910000687	#NAME?	C ₃₁ H ₃₃ F ₃ N ₂ O ₄ 554.606
9100	704	1	000726087	9100-009 H 09	0.399	54.38	Spy4H	0.1776	TR0910000704	#NAME?	C ₃₃ H ₃₇ F ₃ N ₂ O ₃ 566.66
9100	3758	1	000728901	9100-051 F 11	0.285	54.27	Spy4H	0.1776	TR0910003758	#NAME?	C ₃₅ H ₄₁ N ₃ O ₅ 583.725
9100	1062	1	000726445	9100-014 F 04	0.258	54.18	Spy4H	0.1776	TR0910001062	#NAME?	C ₂₈ H ₃₆ N ₂ O ₄ 464.602

Library	Cmpd ID	Exp Req.	Plate	Well	Raw Data	Assay Result	Assay	Conc ng/ml	LionID	#NAME?	
9100	1694	1	000726837	9100-023	F 03	0.304	54.15	0.1776	TR0910001694	C ₂₈ H ₃₃ BrN ₄ O ₃	553.498
9100	2525	1	000727668	9100-036	E 07	0.325	54.11	Spy4H	0.1776	TR0910002525	#NAME?
9100	2742	1	000727785	9100-039	F 04	0.4	54.06	Spy4H	0.1776	TR0910002742	#NAME?
9100	2211	1	000727354	9100-031	C 08	0.323	54.05	Spy4H	0.1776	TR0910002211	#NAME?
9100	1694	1	000727668	9100-036	E 07	0.325	54.11	Spy4H	0.1776	TR0910002525	#NAME?
9100	2742	1	000727785	9100-039	F 04	0.4	54.06	Spy4H	0.1776	TR0910002742	#NAME?
9100	2211	1	000727354	9100-031	C 08	0.323	54.05	Spy4H	0.1776	TR0910002211	#NAME?
9100	1694	1	000727668	9100-036	E 07	0.325	54.11	Spy4H	0.1776	TR0910002525	#NAME?
9100	2742	1	000727785	9100-039	F 04	0.4	54.06	Spy4H	0.1776	TR0910002742	#NAME?
9100	2211	1	000727354	9100-031	C 08	0.323	54.05	Spy4H	0.1776	TR0910002211	#NAME?

LionID	Chira	Lot	E	Reg	Plate	Well	Raw Data	Assay Result	Assay Concentration	LionID	#NAME?	C ₃₃ H ₃₇ N ₃ O ₄	539.672
9100	3723	1	000728866	9100-051	C 07	0.28	53.97	Spy4H	0.1776	TR0910003723	#NAME?	C ₂₉ H ₃₇ N ₃ O ₃	475.629
9100	1069	1	000726452	9100-014	E 05	0.259	53.90	Spy4H	0.1776	TR0910001069	#NAME?	C ₂₉ H ₃₇ N ₃ O ₃	475.629
9100	1732	1	000726875	9100-023	D 08	0.333	53.88	Spy4H	0.1776	TR0910001732	#NAME?	C ₃₂ H ₂₉ F N ₂ O ₃	508.59
9100	4396	1	000729539	9100-060	D 11	0.347	53.87	Spy4H	0.1776	TR0910004396	#NAME?	C ₃₁ H ₃₄ N ₂ O ₄	498.62

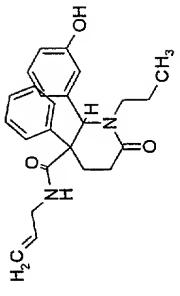
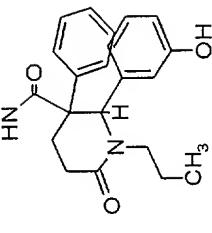
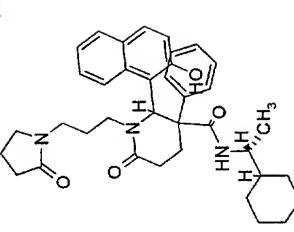
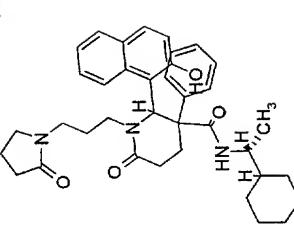
Libran	Cmpd	Loc	ExtReg	Plate	Well	Raw Data	Assay Result	Conc mg/ml	LionID	
9100	571	1	000725954	9100-008	C 03	0.395	53.80	0.1776	TR0910000571	#NAME?
9100	636	1	000726019	9100-008	D 11	0.278	53.80	Spy4H	0 1776	TR0910000636
9100	3253	1	000728396	9100-045	E 08	0 283	53.78	Spy4H	0.1776	TR0910003253
9100	708	1	000726091	9100-009	D 10	0.306	53.71	Spy4H	0.1776	TR0910000708
										#NAME?
										C ₃₀ H ₃₂ F N ₃ O ₅
										533.597
										#NAME?
										C ₃₀ H ₃₄ N ₂ O ₃
										470.61
										C ₂₈ H ₃₀ N ₂ O ₄
										458.555

Library	Compd	Lo.	ExReg	Plate	Well	Raw Data	Assay Result	Assay	Conc	mg/ml	LionID		
9100	2603	1	000727746	9100-037	C 07	0.467	53.70	Spy4H	0.1776	TR0910002603	#NAME?	C ₃₁ H ₃₃ Cl N ₂ O ₃	517.066
9100	2414	1	000727557	9100-035	F 03	0.258	53.59	Spy4H	0.1776	TR0910002414	#NAME?	C ₃₃ H ₃₆ N ₄ O ₃	536.672
9100	1949	1	000727092	9100-028	E 05	0.281	53.49	Spy4H	0.1776	TR0910001949	#NAME?	C ₃₁ H ₄₁ N ₃ O ₄	519.682

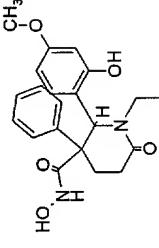
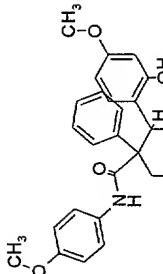
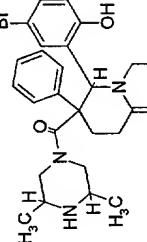
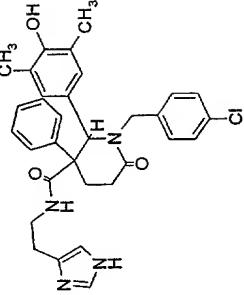
Libary	Cmpd	Loc	ExReg	Plate	Well	Raw Data	Assay	Result	Assay	Conc	Unit	LionID	
9100	998	1	000726381	9100-013	F 06	0.276	53.46	Spy4H	0.1776	TR0910000998	#NAME?	C ₃₁ H ₃₈ BrN ₃ O ₅	612.561
9100	765	1	000726148	9100-010	E 07	0.252	53.41	Spy4H	0.1776	TR0910000765	#NAME?	C ₂₈ H ₃₄ N ₂ O ₃	446.588
9100	3756	1	000728899	9100-051	D 11	0.288	53.36	Spy4H	0.1776	TR0910003756	C ₃₆ H ₃₇ N ₃ O ₅	591.704	

Liber	Cmpd	Lo	ExReg	Plate	Well	Raw Data	Assay Result	Assay	Conc	mg/ml	LionID		
9100	3213	1	000728356	9100-045	E 03	0.422	53.24	Spy4H	0.1776	TR0910003213	#NAME?	C ₃₀ H ₃₁ F N ₂ O ₃	486.584
9100	2205	1	000727348	9100-031	E 07	0.27	53.24	Spy4H	0.1776	TR0910002205	#NAME?	C ₃₅ H ₄₁ N ₃ O ₃	551.727
9100	2236	1	000727379	9100-031	D 11	0.276	53.24	Spy4H	0.1776	TR0910002236	#NAME?	C ₃₇ H ₃₉ N ₃ O ₄	589.732
9100	629	1	000726012	9100-008	E 10	0.258	53.22	Spy4H	0.1776	TR0910000629	#NAME?	C ₂₇ H ₃₅ N ₃ O ₃	449.591

Liber	Cmpd	Lo	ExPeg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	#NAME?	C ₂₈ H ₃₀ N ₂ O ₃ S	474.622	
9100	1058	1	000726441	9100-014	B 04	0.351	53.05	Spy4H	0.1776	TR0910001058	#NAME?			
9100	1068	1	000726451	9100-014	D 05	0.261	53.05	Spy4H	0.1776	TR0910001068	#NAME?			450.576
9100	598	1	000725981	9100-008	F 06	0.264	52.93	Spy4H	0.1776	TR0910000598	#NAME?			464.602
9100	2573	1	000727716	9100-037	E 03	0.287	52.84	Spy4H	0.1776	TR0910002573	#NAME?			591.723

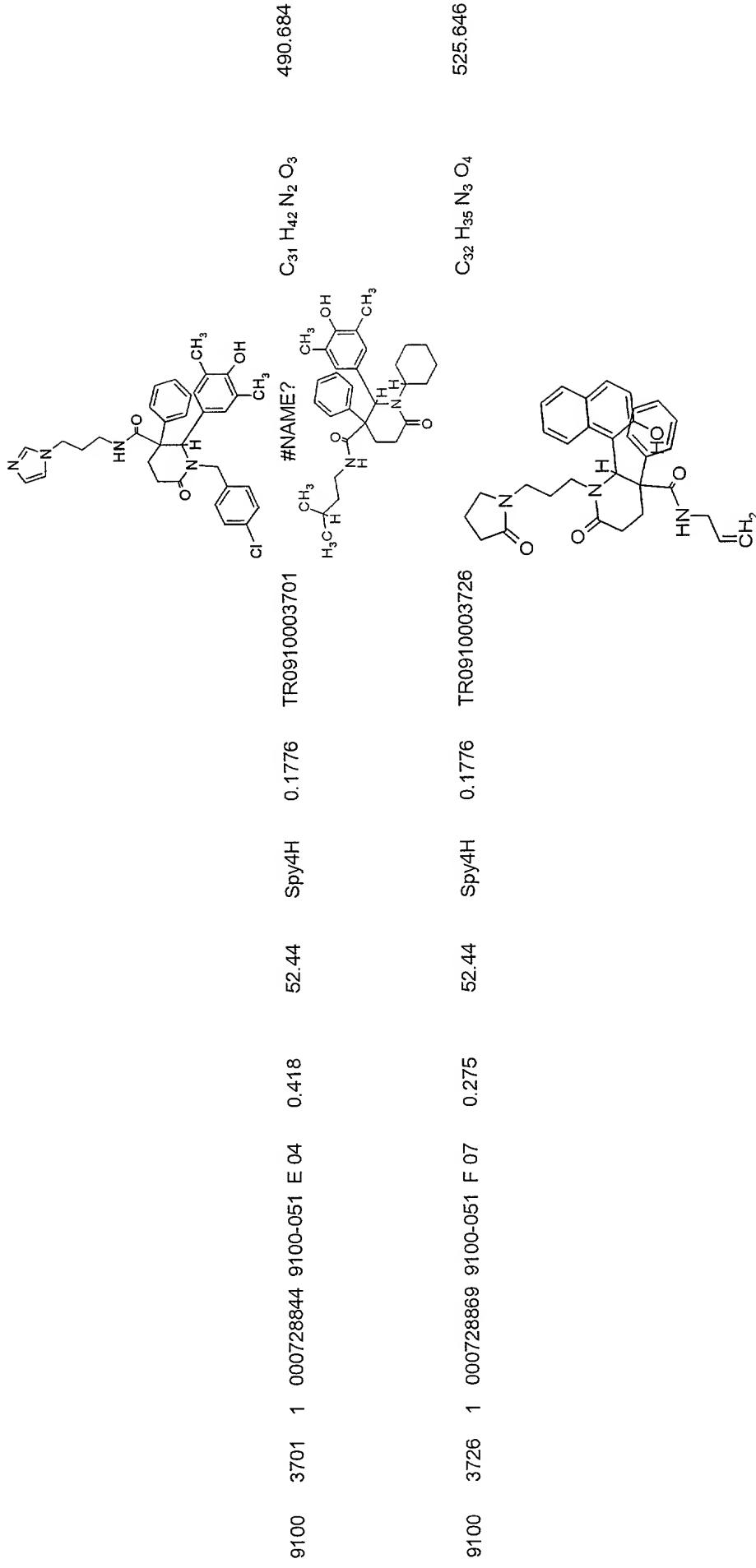
LionID	Cmpd	Loc	ExPreg	Plate	Well	Raw Data	Assay Result	Conc mg/ml	LionID	#NAME?	Chemical Structure	MW
9100	1086	1	000726469	9100-014	F 07	0.263	52.76	Spy4H	0.1776	TR0910001086		392.496
9100	1098	1	000726481	9100-014	B 09	0.298	52.76	Spy4H	0.1776	TR0910001098		448.584
9100	3743	1	000728886	9100-051	G 09	0.347	52.75	Spy4H	0.1776	TR0910003743		595.779
9100										Compound		595.779

Lipiany	Compd Lot	ExReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	
9100	812	1	000726195	9100-011 D	03	0.339	52.70	Spy4H	0.1776	TR0910000812
9100	2196	1	000727339	9100-031 D	06	0.271	52.69	Spy4H	0.1776	TR0910002196
9100	2220	1	000727363	9100-031 D	09	0.269	52.69	Spy4H	0.1776	TR0910002220
9100	2437	1	000727580	9100-035 E	06	0.261	52.63	Spy4H	0.1776	TR0910002437
								#NAME?		
								#NAME?		
								#NAME?		
								#NAME?		
								#NAME?		
								C ₂₇ H ₂₈ N ₂ O ₄		444.528
								C ₃₁ H ₃₅ FN ₂ O ₅		534.625
								C ₃₁ H ₃₅ N ₃ O ₆		529.633

Library	Cmpd	Lot	ExReg	Plate	Well	Raw Data	Assay Result	Assay	Conc ng/ml	LionID	
9100	2757	1	000727900	9100-039	E 06	0.359	52.61	Spy4H	0.1776	TR0910002757	#NAME?
											
9100	2396	1	000727539	9100-033	D 11	0.334	52.60	Spy4H	0.1776	TR0910002396	#NAME?
											
9100	229	1	000725612	9100-003	E 10	0.266	52.55	Spy4H	0.1776	TR0910000229	#NAME?
											
9100	2604	1	000727747	9100-037	D 07	0.267	52.55	Spy4H	0.1776	TR0910002604	#NAME?
											

9100 2614 1 000727757 9100-037 F 08 0.317 52.55 Spy4H 0.1776 TR0910002614

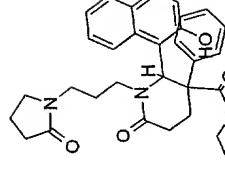
Lipian	Compd	Loc	Exptg	Plate	Well	Raw Data	Assay Result	Assay Concn	LionID	#NAME?	C ₃₃ H ₃₅ ClN ₄ O ₃	571.117	
9100	2614	1	000727757	9100-037	F 08	0.317	52.55	Spy4H	0.1776	TR0910002614	#NAME?	C ₃₃ H ₃₅ ClN ₄ O ₃	571.117



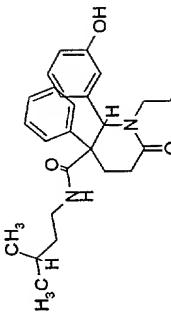
LionID Cmpd Lot ExReg Plate Well Run Data Assay Result Assay Config ID LionID

9100 3755 1 000728898 9100-051 C 11 0.294 52.44 Spy4H 0.1776 TR0910003755

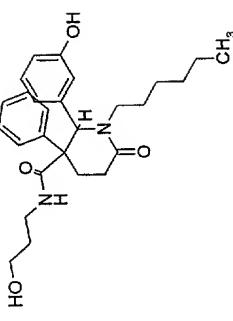
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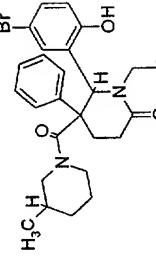
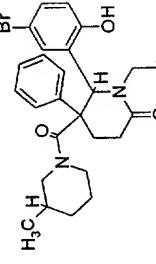
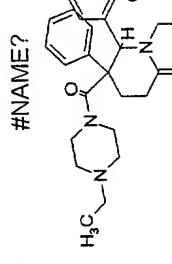
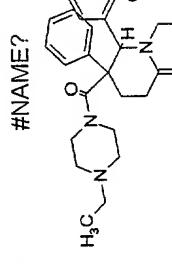
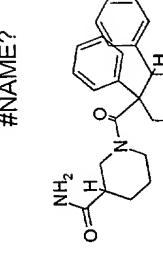
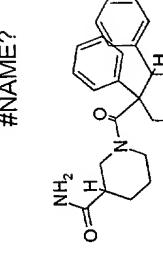
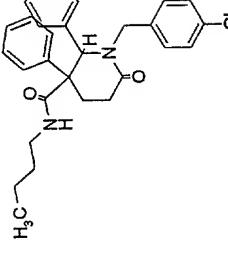
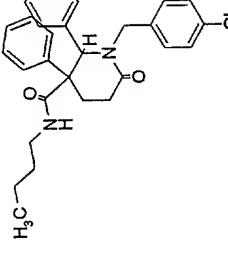
9100 1021 1 000726404 9100-013 E 09 0.399 52.37 Spy4H 0.1776 TR0910001021 #NAME? C₂₉H₄₀N₂O₃ 464.646

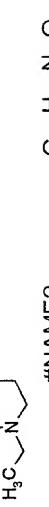
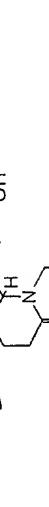
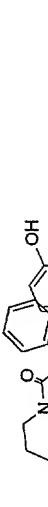


9100 1027 1 000726410 9100-013 C 10 0.28 52.37 Spy4H 0.1776 TR0910001027 #NAME? C₂₇H₃₆N₂O₄ 452.591



Library	Chip	Loc	Ex Reg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	#NAME?	C ₃₄ H ₃₅ F ₃ N ₄ O ₃	604.669
9100	694	1	000726077	9100-009	F 08	0.285	52.36	Spy4H	0.1776	TR0910000694	#NAME?		
9100	579	1	000725962	9100-008	C 04	0.261	52.35	Spy4H	0.1776	TR0910000579	H ₃ C,N #NAME?	C ₂₇ H ₃₇ N ₃ O ₃	451.607
9100	603	1	000725986	9100-008	C 07	0.269	52.35	Spy4H	0.1776	TR0910000603	H ₃ C,N #NAME?	C ₂₅ H ₃₀ N ₂ O ₃	406.523
9100	4123	1	000729266	9100-057	C 07	0.289	52.30	Spy4H	0.1776	TR0910004123	H ₃ C,N #NAME?	C ₃₆ H ₄₃ N ₃ O ₃	565.754

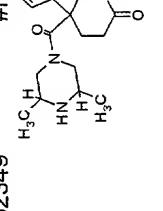
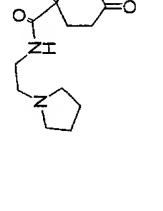
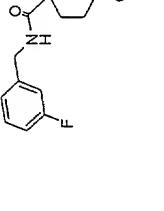
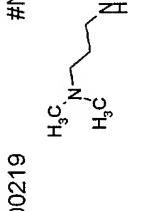
Library	Compd	Loc	Expt Reg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	#NAME?	C ₂₇ H ₃₁ Br N ₂ O ₃	511.457	
9100	235	1	000725618	9100-003	C 11	0.485	52.25	Spy4H	0.1776	TR0910000235			C ₂₇ H ₃₁ Br N ₂ O ₃	511.457
9100	820	1	000726203	9100-011	D 04	0.272	52.16	Spy4H	0.1776	TR0910000820			#NAME?	523.67
9100	841	1	000726224	9100-011	A 07	0.354	52.16	Spy4H	0.1776	TR0910000841			#NAME?	546.064
9100	872	1	000726255	9100-011	H 10	0.406	52.16	Spy4H	0.1776	TR0910000872			#NAME?	491.028

Library	Cmd	Loc	ExReg	Plate	Well	RawData	Assay	Conc	LionID	
9100	3740	1	00072883	9100-051 D 09	0.275	52.14	Spy4H	0.1776	TR09100003740	#NAME?
9100	580	1	000725963	9100-008 D 04	0.263	52.06	Spy4H	0.1776	TR0910000580	
9100	604	1	000725987	9100-008 D 07	0.261	52.06	Spy4H	0.1776	TR0910000604	
9100	707	1	000726090	9100-009 C 10	0.306	52.02	Spy4H	0.1776	TR0910000707	
9100	582	1	000726090	9100-009 C 04	0.275	52.14	Spy4H	0.1776	TR0910000804	

Lipian	Compound ID	Lot	Expt Reg.	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID		
9100	4084	1	000729227	9100-057	D 02	0.264	52.02	Spy4H	0.1776	TR0910004084	#NAME?	C ₃₁ H ₂₉ F ₃ N ₄ O ₃
9100	733	1	000726116	9100-010	E 03	0.253	51.92	Spy4H	0.1776	TR0910000733	#NAME?	C ₂₇ H ₂₇ F N ₂ O ₃
9100	578	1	000725961	9100-008	B 04	0.334	51.77	Spy4H	0.1776	TR0910000578	#NAME?	C ₂₇ H ₃₀ N ₂ O ₃ S
9100	586	1	000725969	9100-008	B 05	0.301	51.77	Spy4H	0.1776	TR0910000586	#NAME?	C ₂₆ H ₃₄ N ₂ O ₃
												446.519
												462.611
												422.566
												562.589

Library	Cmpd_1	Expres	Plate	Well	Ray Date	Assay Result	Assay	Conc/mM	LionID		
9100	628	1	000726011	9100-008 D	10	0.263	51.77	Spy4H	0.1776	TR0910000628	#NAME?
											C ₂₅ H ₃₂ N ₂ O ₄
											424.538
9100	630	1	000726013	9100-008 F	10	0.264	51.77	Spy4H	0.1776	TR0910000630	#NAME?
											390.48
9100	2977	1	000728120	9100-042 A	04	0.341	51.75	Spy4H	0.1776	TR0910002977	#NAME?
											C ₂₈ H ₂₈ Cl ₂ N ₂ O ₄
9100	1695	1	000726838	9100-023 G	03	0.442	51.74	Spy4H	0.1776	TR0910001695	#NAME?
											C ₂₆ H ₂₉ Br N ₂ O ₃
											485.419

Library	Compound ID	Lot	Expt Reg.	Plate	Well	Raw Data	Assay Result	Assay	Canc. gfm	LionID	#NAME?	
9100	683	1	000726066	9100-009	C 07	0.546	51.69	Spy4H	0.1776	TR0910000683	C ₃₂ H ₃₃ F ₃ N ₂ O ₃	550.618
9100	1939	1	000727082	9100-028	C 04	0.287	51.58	Spy4H	0.1776	TR0910001939	#NAME?	507.671
9100	1956	1	000727099	9100-028	D 06	0.29	51.58	Spy4H	0.1776	TR0910001956	#NAME?	528.645
											C ₃₂ H ₃₆ N ₂ O ₆	

LionID	Chg#	Lot#	ExReg	Plate	Wst#	Raw Date	Assay Result	Assay	Conc mg/ml	LionID	#NAME?	C ₂₇ H ₃₄ N ₂ O ₃	434.577
9100	1015	1	000726398	9100-013	G 08	0.352	51.56	Spy4H	0.1776	TR0910001015	#NAME?		
9100	2349	1	000727492	9100-033	E 05	0.299	51.48	Spy4H	0.1776	TR0910002349		C ₃₂ H ₄₃ N ₃ O ₄	533.709
9100	4122	1	000729265	9100-057	B 07	0.273	51.46	Spy4H	0.1776	TR0910004122		C ₃₈ H ₄₈ N ₄ O ₃	608.822
9100	2532	1	000727675	9100-036	D 08	0.323	51.44	Spy4H	0.1776	TR0910002532		C ₃₂ H ₃₇ F N ₂ O ₅	548.651
9100	219	1	000725602	9100-003	C 09	0.265	51.33	Spy4H	0.1776	TR0910000219		#NAME?	

Lipian	Compd	Lot	ExReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	#NAME?	C ₃₀ H ₃₈ BrN ₃ O ₅	600.55
9100	982	1	000726365	9100-013 F 04	0.28	51.29	Spy4H	0.1776	TR0910000982	#NAME?			
9100	3742	1	000728885	9100-051 F 09	0.276	51.22	Spy4H	0.1776	TR0910003742	H ₃ C	#NAME?	C ₃₄ H ₄₁ N ₃ O ₆	571.714
9100	2982	1	000728125	9100-042 F 04	0.438	51.21	Spy4H	0.1776	TR0910002982	H ₃ C	#NAME?	C ₃₁ H ₃₄ Cl ₂ N ₂ O ₄	569.526

LionID	Cmpd Lot	Entrez	Plate	Well	Raw Data	Assay Result	Assay Concentration	LionID	#NAME?	Chemical Structure	Molecular Formula	Mass
9100	1758	1	000726901	9100-023 F 11	0.298	51.20	Spy4H	0.1776	TR0910001758	#NAME?	C ₃₁ H ₃₄ N ₂ O ₄	498.62
9100	2365	1	000727508	9100-033 E 07	0.34	51.19	Spy4H	0.1776	TR0910002365	#NAME?	C ₂₇ H ₃₂ N ₂ O ₄	448.56
9100	588	1	000725971	9100-008 D 05	0.267	51.19	Spy4H	0.1776	TR0910000588	#NAME?	C ₂₆ H ₃₄ N ₂ O ₄	438.565
9100	620	1	000726003	9100-008 D 09	0.264	51.19	Spy4H	0.1776	TR0910000620	#NAME?	C ₂₇ H ₃₅ N ₃ O ₃	449.591

Library	ChIPd	Lot	ExPReg	Plate	Well	Raw Data	Assay	Result	Conc mg/ml	LionID	#NAME?	C ₂₉ H ₃₀ Cl ₂ N ₂ O ₄	541.472
9100	2519	1	000727662	9100-036	G 06	0.383	51.17	Spy4H	0.1776	TR0910002519	#NAME?		
9100	1060	1	000726443	9100-014	D 04	0.269	51.06	Spy4H	0.1776	TR0910001060	#NAME?		
9100	2203	1	000727346	9100-031	C 07	0.277	51.06	Spy4H	0.1776	TR0910002203	#NAME?		
9100	2413	1	000727556	9100-035	E 03	0.49	51.02	Spy4H	0.1776	TR0910002413	#NAME?		

LiparID	Cmpd ID	Lot	Expt Reg	Plate	Well	Raw Data	Assay Result	Assay Concentration	LionID	#NAME?	Chemical Structure	Chemical Formula	MW
9100	2466	1	000727609	9100-035	B 10	0.394	51.02	Spy4H	0.1776	TR0910002466		C ₂₈ H ₃₇ BrN ₂ O ₃	529.515
9100	965	1	000726348	9100-013	E 02	0.337	51.02	Spy4H	0.1776	TR0910000965		#NAME?	582.535
9100	1697	1	000726840	9100-023	A 04	0.363	50.94	Spy4H	0.1776	TR0910001697		#NAME?	489.407
9100	1697	1	000726840	9100-023	A 04	0.363	50.94	Spy4H	0.1776	TR0910001697		C ₂₄ H ₂₉ BrN ₂ O ₄	489.407

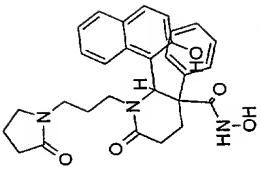
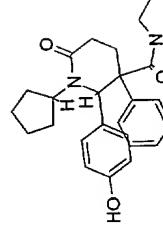
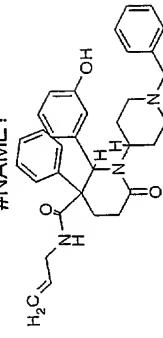
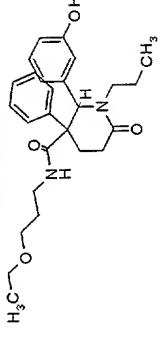
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9100	1715	1	000726858	9100-023	C 06	0.557	50.94	Spy4H	0.1776	TR0910001715	C ₂₈ H ₃₅ Br N ₂ O ₃	527.5	
9100	3033	1	000728176	9100-042	A 11	0.445	50.94	Spy4H	0.1776	TR0910003033	#NAME?		
9100	3691	1	000728834	9100-051	C 03	0.457	50.92	Spy4H	0.1776	TR0910003691	C ₂₉ H ₄₀ N ₂ O ₅	496.644	
9100	3748	1	000728891	9100-051	D 10	0.275	50.92	Spy4H	0.1776	TR0910003748	#NAME?		
											C ₃₄ H ₄₀ N ₂ O ₃	524.701	
											C ₃₃ H ₃₉ N ₃ O ₅	557.687	

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Library	Chpd	Exp#	Plate	Well	Raw Data	Assay Result	Assay	Conc.mg/ml	LionID	#NAME?	CH ₃	C ₂₉ H ₂₉ FN ₂ O ₄
9100	2373	1	000727516	9100-033	E 08	0.351	50.91	Spy4H	0.1776	TR09100002373	#NAME?	
9100	606	1	000725989	9100-008	F 07	0.266	50.90	Spy4H	0.1776	TR0910000606	#NAME?	
9100	618	1	000726001	9100-008	B 09	0.291	50.90	Spy4H	0.1776	TR0910000618	#NAME?	
9100	2795	1	000727938	9100-039	C 11	0.392	50.87	Spy4H	0.1776	TR0910002795	#NAME?	

Library	Compd	Lot	Expt#	Plate	Well	Raw Data	Assay	Result	Assay	Conc	mg/ml	LionID	#NAME?	C ₃₂ H ₃₇ ClN ₂ O ₄	549.107
9100	2622	1	000727765	9100-037	F 09	0.377	50.83	Spy4H	0.1776	TR0910002622				C ₂₄ H ₂₆ N ₂ O ₃	390.48
9100	1110	1	000726493	9100-014	F 10	0.272	50.78	Spy4H	0.1776	TR0910001110				C ₃₁ H ₃₅ FN ₂ O ₃	502.626
9100	1012	1	000726395	9100-013	D 08	0.517	50.75	Spy4H	0.1776	TR0910001012				C ₃₃ H ₃₇ N ₃ O ₄	539.672
9100	2401	1	000727544	9100-035	A 02	0.33	50.70	Spy4H	0.1776	TR0910002401					

Library	Cmpd_#	ExptReg	Plate	Well	Raw Data	Assay Result	Conc/mi	LionID		
9100	2426	1	000727569	9100-035	B 05	0.324	50.70	Spy4H	0.1776	TR0910002426
									#NAME?	C ₃₁ H ₃₆ N ₂ O ₃
										484.636
9100	1687	1	000726830	9100-023	G 02	0.338	50.67	Spy4H	0.1776	TR0910001687
										#NAME?
										C ₂₅ H ₃₁ Br N ₂ O ₄
										503.434
9100	2342	1	000727485	9100-033	F 04	0.32	50.63	Spy4H	0.1776	TR0910002342
										#NAME?
										C ₃₁ H ₄₂ N ₂ O ₅
										522.682
9100	626	1	000726009	9100-008	B 10	0.284	50.62	Spy4H	0.1776	TR0910000626
										#NAME?
										C ₂₅ H ₃₂ N ₂ O ₃
										408.539

Library	Chemical Reg.	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	#NAME?	Chemical Structure	Molecular Formula	Mass
9100	3757 1	000728900	9100-051 E 11	0.272	50.61	Spy4H	0.1776	TR0910003757	#NAME?		C ₂₉ H ₃₁ N ₃ O ₅	501.58
9100	2763 1	000727906	9100-039 C 07	0.322	50.58	Spy4H	0.1776	TR0910002763	#NAME?		C ₂₇ H ₃₂ N ₂ O ₃	432.561
9100	2206 1	000727349	9100-031 F 07	0.277	50.51	Spy4H	0.1776	TR0910002206	#NAME?		C ₃₃ H ₃₇ N ₃ O ₃	523.673
9100	1102 1	000726485	9100-014 F 09	0.271	50.50	Spy4H	0.1776	TR0910001102	#NAME?		C ₂₆ H ₃₄ N ₂ O ₄	438.565

Library	Compound ID	EXPERG	Plate	Well	Frac Data	Assay Result	Conc mg/ml	LionID		
9100	2430	1	000727573	9100-035 F 05	0.288	50.38	Spy4H	0.1176	TR0910002430	#NAME?
										C ₃₀ H ₃₀ N ₂ O ₃
										466.578
9100	717	1	000726100	9100-009 E 11	0.252	50.34	Spy4H	0.1776	TR0910000717	#NAME?
										512.525
9100	2204	1	000727347	9100-031 D 07	0.278	50.24	Spy4H	0.1776	TR0910002204	#NAME?
										577.725
9100	2219	1	000727362	9100-031 C 09	0.282	50.24	Spy4H	0.1776	TR0910002219	#NAME?
										C ₃₅ H ₃₉ N ₅ O ₃
										568.758

Library	Compound ID	Lot	Expt #	Plate	Well	Raw Data	Assay Result	Assay	Config/fit	LionID	Conc (ug/ml)	#NAME?		
9100	1059	1	000726442	9100-014	C 04	0.273	50.21	Spy4H	0.1776	TR0910001059	H ₃ C ₂ N(C ₂ H ₅)C ₂ H ₅	C ₂₈ H ₃₇ N ₃ O ₃	463.618	
9100	1109	1	000726492	9100-014	E 10	0.273	50.21	Spy4H	0.1776	TR0910001109	H ₃ C ₂ N(C ₂ H ₅)C ₂ H ₅	#NAME?	C ₂₇ H ₃₅ N ₃ O ₃	449.591
9100	1981	1	000727124	9100-028	E 09	0.283	50.21	Spy4H	0.1776	TR0910001981	H ₃ C ₂ N(C ₂ H ₅)C ₂ H ₅	#NAME?	C ₂₈ H ₃₈ N ₂ O ₄	466.618
9100	974	1	000726357	9100-013	F 03	0.28	50.20	Spy4H	0.1776	TR0910000974	C ₃₁ H ₃₆ BrN ₅ O ₄		622.56	

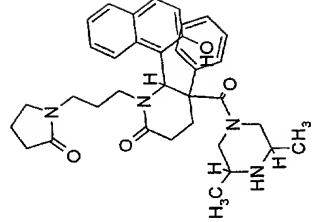
Library	Comp	Loc	ExReg	Plate	Well	RawData	Assay	Result	Assay	Conc(mg/ml)	LionID		
9100	1686	1	000726829	9100-023	F 02	0.427	50.13	Spy4H	0.1776	TR09100001686	#NAME?	C ₂₅ H ₂₉ BrN ₂ O ₃	485.419
9100	2493	1	000727636	9100-036	E 03	0.532	50.10	Spy4H	0.1776	TR09100002493	#NAME?	C ₃₅ H ₃₃ Cl ₂ FN ₂ O ₃	619.561
9100	587	1	000725970	9100-008	C 05	0.273	50.04	Spy4H	0.1776	TR0910000587	#NAME?	C ₂₅ H ₃₂ N ₂ O ₄	424.538
9100	828	1	000726211	9100-011	D 05	0.28	50.00	Spy4H	0.1776	TR0910000828	#NAME?	C ₂₈ H ₃₈ N ₂ O ₆	498.616

9100 3749 1 000728892 9100-051 E 10 0.28 50.00 Spy4H 0.1776 TR09100003749

582.741

C₃₅H₄₂N₄O₄

#NAME?



EXAMPLE 4

Melanocortin Receptor Assay

[0124] This example describes methods for assaying binding to MC receptors.

[0125] All cell culture media and reagents are obtained from GibcoBRL (Gaithersburg MD), except for COSMIC CALF SERUM (HyClone; Logan UT). HEK 293 cell lines are transfected with the human MC receptors hMCR-1, hMCR-3, and hMCR-4 (Gantz et al., Biochem. Biophys. Res. Comm. 200:1214-1220 (1994); Gantz et al., J. Biol. Chem. 268:8246-8250 (1993); Gantz et al. J. Biol. Chem. 268:15174-15179 (1993); Haskell-Leuvano et al., Biochem. Biophys. Res. Comm. 204:1137-1142 (1994); each of which is incorporated herein by reference). Vectors for construction of an hMCR-5 expressing cell line are obtained, and a line of HEK 293 cells expressing hMCR-5 is constructed (Gantz, *supra*, 1994). hMCR-5 has been described previously (Franberg et al., Biochem. Biophys. Res. Commun. 236:489-492 (1997); Chowdhary et al., Cytogenet. Cell Genet. 68:1-2 (1995); Chowdhary et al., Cytogenet. Cell Genet. 68:79-81 (1995), each of which is incorporated herein by reference). HEK 293 cells are maintained in DMEM, 25 mM HEPES, 2 mM glutamine, non-essential amino acids, vitamins, sodium pyruvate, 10% COSMIC CALF SERUM, 100 units/ml penicillin, 100 µg/ml streptomycin and 0.2 mg/ml G418 to maintain selection.

[0126] Before assaying, cells are washed once with phosphate buffered saline ("PBS"; without Ca²⁺ and Mg²⁺), and stripped from the flasks using 0.25% trypsin and 0.5 mM EDTA. Cells are suspended in PBS, 10% COSMIC CALF SERUM and 1 mM CaCl₂. Cell suspensions are prepared at a density of 2x10⁴ cells/ml for HEK 293 cells expressing hMCR-3, hMCR-4 or hMCR-5, and 1x10⁵ cells/ml for HEK 293 cells expressing hMCR-1. Suspensions are placed in a water bath and allowed to warm to 37°C for 1 hr.

[0127] Binding assays are performed in a total volume of 250 µl for HEK 293 cells. Control and test compounds are dissolved in distilled water. ¹²⁵I-HP 467 (50,000 dpm) (2000 Ci/mmol) (custom labeled by Amersham; Arlington Heights IL) is prepared in 50 mM Tris, pH 7.4, 2 mg/ml BSA, 10 mM CaCl₂, 5 mM MgCl₂,

2 mM EDTA and added to each tube. To each tube is added 4x103 HEK 293 cells expressing hMCR-3, hMCR-4 or hMCR-5, or 2x104 cells expressing hMCR-1. Assays are incubated for 2.5 hr at 37°C.

[0128] GF/B filter plates are prepared by soaking for at least one hour in 5 mg/ml BSA and 10 mM CaCl₂. Assays are filtered using a Brandel 96-well cell harvester (Brandel Inc.; Gaithersburg, MD). The filters are washed four times with cold 50 mM Tris, pH 7.4, and the filter plates dehydrated for 2 hr and 35 µl of MICROSCINT is added to each well. Filter plates are counted using a Packard Topcount (Packard Instrument Co.) and data analyzed using GraphPad PRISM v2.0 (GraphPad Software Inc.; San Diego CA) and Microsoft EXCEL v5.0a (Microsoft Corp.; Redmond WA).

[0129] To assay piperidine-3-carboxamide derivative compounds, binding assays are performed in duplicate in a 96 well format. HP 467 is prepared in 50 mM Tris, pH 7.4, and ¹²⁵I-HP 467 is diluted to give 100,000 dpm per 50 µl. A piperidine-3-carboxamide derivative compound, is added to the well in 25 µl aliquots. A 25 µl aliquot of ¹²⁵I-HP 467 is added to each well. A 0.2 ml aliquot of suspended cells is added to each well to give the cell numbers indicated above, and the cells are incubated at 37°C for 2.5 hr. Cells are harvested on GF/B filter plates as described above and counted.

EXAMPLE 5

Penile erection due to administration of a piperidine-3-carboxamide derivative compounds

[0130] Adult male rats are housed 2-3 per cage and are acclimated to the standard vivarium light cycle (12 hr. light, 12 hr. dark), rat chow and water for a least a week prior to testing. All experiments are performed between 9 a.m. and noon and rats are placed in cylindrical, clear plexiglass chambers during the 60 minute observation period. Mirrors are positioned below and to the sides of the chambers, to improve viewing.

[0131] Observations begin 10 minutes after an intraperitoneal injection of either saline or compound. An observer counts the number of grooming motions,

stretches, yawns and penile erections (spontaneously occurring, not elicited by genital grooming) and records them every 5 minutes, for a total of 60 minutes. The observer is unaware of the treatment and animals are tested once, with n=6 in each group. Values in the figures represent the group mean and standard error of the mean. HP 228 can be used as a positive control for penile erections. Significant differences between groups are determined by an overall analysis of variance and the Student Neunmann-Keuls post hoc test can be used to identify individual differences between groups ($p \leq 0.05$).

[0132] Although the invention has been described with reference to the examples provided above, it should be understood that various modifications can be made by those skilled in the art without departing from the invention. Accordingly, the invention is set out in the following claims.